

The Indian Physician

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WHOLE No 1

ABOUT OURSELVES

There are so many medical journals in existence that an explanation is necessary to justify the appearance of one more. For long, we have felt the need for a journal of internal medicine confining itself to the problems presenting to the practising physicians in India. The journals published in India at present are devoted either to pure research work, or to serve the requirements of the general practitioners. In India there are a number of Universities preparing students for graduate and post-graduate degrees. There are a number of hospitals where there is a wealth of clinical material, and we have felt for a long time the need of tapping this. The text books used by students and practitioners are written by foreign writers, and little is mentioned there about local conditions in India. There is a need for a clinical journal which will publish diseases peculiar to India, and also classical diseases described by Western writers, but modified by Indian conditions. Again there is a great need for critical review of recent literature published throughout the world in relation to its applicability to the Indian conditions. The medical literature is so extensive that no one man can aspire to master it as a whole, it is necessary to have a critical selection and sifting of the material, without such critical appraisement much of the literature is more often than not premature or misleading.

We hope this journal will meet this need and foster a critical and scientific attitude in the practising physicians, and encourage them to make clinical observations and exchange their experiences.

A word about our title 'The Indian Physician' does not mean a physician practising Indigenous Medicine. Practitioners

of Indigenous Medicine are either Ayurvedic or Yunani. If any physician has a right to call himself an Indian physician, it is the practitioner of Modern Scientific Medicine. He is not bound by any narrow system of medicine. He is free to take anything which appeals to his reason from anywhere in the world. He follows the modern experimental method of science. Observation of facts, experimental verification, and workability of hypothesis are his guiding lights rather than an appeal to authority, or this or that theory or belief of the past, hallowed by religion or nationality. We are convinced that the so called revival of the schools of Indigenous Medicine by the National Provincial Governments is a retrograde step, one might as well revive the medieval beliefs in magic, alchemy, astrology, and what not. This is not to suggest that there is nothing good in the ancient systems of medicine. Perhaps there is a great deal of worth there, but this could have been very well found out by instituting chairs of Indigenous Medicine in several Universities to study these systems by modern scientific methods and to incorporate in the body of modern medical knowledge whatever good is found in the ancient systems of practice.

Modern Scientific Medicine is not national, it is international, it is not a closed system, it is always willing to incorporate within itself whatever satisfies its experimental tests. Eddington some years ago while giving a lecture, entitled *The Expanding Universe*, showed the international character of the physical sciences in the following words:

"I shall speak of the theoretical work of Einstein of Germany, de Sitter of Holland, Lemaitre of Belgium. For observational data I turn to the Americans, Shipher, Hubble, Humason, recalling, however, that the vitally important datum of distance is found by a method which we owe to Hertzprung of Denmark. As I must not trouble you with mathematical analysis, I have to pass over Levi-Civita of Italy, whose methods and ideas we employ. But I must refer especially to the new interest which arises in the subject through its linkage to wave-mechanics, as a representative name in wave mechanics I mention that of its originator, de Broglie of France. My subject disperses the galaxies, but it unites the earth."

A similar statement can be made about modern medicine with equal justice. No nation can isolate itself. No progress

is possible if the mind is shackled with the authority of this or that system, merely because it is national

This journal will be published each month, and will contain original contributions, describing clinical research work, descriptions of diseases, analysis of hospital records, post-mortem records and cognate medical subjects. It will also contain a number of case-reports described in as much detail as possible. Descriptions of rare diseases or interesting manifestations of common diseases with a review of literature on the subject will be a special feature, and we trust, will prove most useful to the practising physicians. In each issue at least one analytical review dealing with some disease or therapeutic problem will be published. We request various teachers of clinical medicine and hospital physicians, as well as general practitioners to co-operate with us in this and submit their observations for publication. Personal experiences of general practitioners in various localities will no doubt be of great interest to others.

We should not be in the grip of the dead past, nor should we be awed by authority but we may not forget that the past has claims over us. The evolution of modern medicine is a series of successes over false beliefs. The present is the child of the past, and, to understand it properly, a historical outlook is essential. Physicians with such an outlook do not hanker after miracles and are not easily lured away from the scientific path by the false promises of pseudo-science, quackery and the fashionable cults of the day. To encourage this historical outlook, we shall publish from time to time a critical article dealing with some personality of the past, irrespective of his nationality or the system of medicine he practised, or shall review the development of some medical idea, or some therapeutic procedure.

Each month we shall publish critical notes on recent advances, or abstracts of recent literature. These will deal with the natural history of the disease or the methods of diagnosis or the problems in clinical pathology, or with therapeutics. The requirements of the practising physicians will be our guide in the selection of these abstracts or notes.

We shall review books and monographs on physiology, pathology and internal medicine in detail, and if space is available we shall also publish short notices on other works of scientific or

cultural interest to physicians We shall give news of interest about physicians, medical education, society meetings, etc

We hope that this journal may lead to a better understanding amongst the practising physicians all over India, and may in future be instrumental in establishing an Association of Indian Physicians or even an Indian College of Physicians chartered by the state to foster Modern Scientific Medicine

Let us remember...

JEAN FERNEL

(1497-1558)

A Physician Philosopher of the sixteenth century

Jean Fernel was born at Montdidier in 1497. He studied in Paris. Loyola was a costudent with him at the College Ste Barbe. He was a lecturer in philosophy in his college before

he turned to medicine. He was distinguished also in mathematics and had turned with enthusiasm to Astronomy and invented an astrolabe.



“As a physician he was remarkable in more than one respect. Of transcendent reputation for success at the bedside both, with the Court and wealthy as with the poor who flocked to him he was, too, the earliest to draw together into one discipline physiology, calling it for the first time by that name, and holding it to be the necessary intro-

duction to scientific medicine. From his Paris folio of 1542 finely printed by Simon de Colines, the modern text book of physiology starts. In the schools his pre-occupation had been rather with cosmology and Cicero, and Aristotle and Pliny, than with patristic learning. What the physician thought about Nature has in every age reflected much of the instructed opinion of the time. His calling too has always led him to view Nature with man as

its central interest The background of Fernel is on the one hand, the humanistic revival still in the flood and on the other hand religious strife, not least in France, beginning in its bitterness to use fire and sword" (Sherrington)

The period of transition from medieval to modern conditions produced Fernel The invention of gun-powder, printing, and the mariners' compass freed man from the ban of authority and developed individualism, freedom of thought and critical spirit A philosophic study of the Greek medicine was begun and the natural writings of Hippocrates took the place of the medieval dialectics and logic chopping of the Galenists

Fernel was one of the writers of the Institutes of Medicine He wrote many books His chief work, entitled *MEDICINA* appeared in 1544, and at a later date was republished with many additions on special diseases and bore the name of

UNIVERSA MEDICINA

The work, however, contains three parts Seven books treat of physiology, describing the parts and their use, the elements, the temperaments, the spirits and innate heat, the faculties, function and humors, and generation The books of physiology, of which there are three, deal with diseases and their causes, their symptoms and signs, the pulse and the urine Seven other books are devoted to therapeutics and to cures, blood-letting, purging and the action of medicaments as well as their use Fernel was desirous of reforming the study of pathology, in which he included the study of the causes and signs of disease

The compilers of the Institutes of Medicine, including Fernel, studied Galen, Aristotle, the Thomists and the Scotists Indeed, they obtained knowledge wherever it could be found They did an immense service to medicine by bringing together all this knowledge in one body

In his curious little treatise entitled *DE ABDITIS RERUM CAUSIS*, the second book of which treats of pathology, Fernel reviews the epidemic, endemic, virulent, and contagious diseases, and gives descriptions of syphilis, elephantiasis, and rabies, which had been neglected by other writers, he examines their causes and refutes the doctrine of materialistic specificity, he admits that everything coming from without may be the cause of disease, but that, according to the doctrine of Hippocrates, it is within the human body and of the corruption properly belonging to it that disease is born Thus he developed an

ætiological doctrine, which is far removed from that of Galen. It was on the ætiological doctrine that the pathological doctrine of the sixteenth century was based, and so it was on the right road. In Fernel's book the question is lengthily dealt with and he puts forward arguments which could reasonably be discussed to-day. Contagious, epidemic and poisonous diseases do not in fact, spread unless there is a pre-disposition to the disease among the population and each person becomes infected according to his constitution. And lastly all so-called specific remedies are merely antidotes which bring about changes in the constitution. This doctrine endured for a very long time, but underwent successive modifications as time went on (Cumston).

Fernel may be regarded as the classical guide of his century. A short four centuries ago, the world and even the cultured world was steeped in a number of superstitions. Of these the chief were magic and astrology. To understand the attitude of Fernel towards these superstitions, we may quote

"There are remedies of supposed præternatural power which are exhibitions merely of superstition. They are neither divine nor truly magical. They cannot claim their mandate either from temperament or from divine influence. The kind of thing they are? Well, a finger ring, a scrap of writing. How shall such things cry aloud for help to God or to His spirits? How should mere words alone and of themselves avail against disease? In the falling sickness words I have heard used are

Myrrh Caspar brought, thyme Melchior,
And Balthazar brought gold,
Whoso shall bring with him these three
In the name of the kings of old
Cures falling sickness by his piety

For the cure of aching teeth there are the words
You combs and saws and Harrows, you things
With teeth ease the pain in these teeth

Again for inflammation of the eyes a paper tied round the neck bearing the Greek characters R and A. Quaintan fever is treated with a nail from a crucifix wrapped in sheep's wool. For splenic pain a fresh ox-spleen fixed over the place of pain and the physician speaking to the spleen says, 'cure thyself'. To get rid of persistent cough cough into a toad's mouth and cast the

load away" Such a discussion, and written from the faculty in Paris less than 400 years ago, is a finger-post showing the long way thought about such things has travelled since then

"Trusted physician of his age, we see Fernel surrounded by a world of magic and superstition Even he can speak of the 'truly magical' For most, even of the cultured of his time in Nature almost anything might happen What had come down from Egypt, Greece and Rome and from the Arabs, along with truth contained an overplus of untruth Such as it was it was still largely unsifted as to the superstitions The later Middle Ages did, in some measure, grow more critical Magic indeed had become more critical itself It looked to experiment, but experiment little guided as yet by any vision of law *Against this darkness Fernel stood a dignified figure, trying to distinguish between true and false Also a pathetic figure because his means of distinguishing between them were so scant He had his single-handed observation and his honest submission of tradition to the general test of reasonableness He judged as an observant man out to know the truth And there were others with him, though they were few (Sherrington)*

Fernel had some insight about the power of faith Hear this

And there is that Bombastus, he persuades the foolish they have a goblin, an Archæus, in their stomachs which only he can treat Let him assuage the Archæus in his own stomach, for it has a deadly drought Incomprehensible? yes, he shouts two contraries in one breath and with his next two more!

"In the way," remarks Fernel, "if he continues he will sometimes be right" "Basta," cries Cardano, '*the man is ignorant Then likely enough he will make cures*', says Fernel "*There ignorance may help It has confidence in itself and that in turn wins confidence from others I have seen the so-called magical work a cure when helped by confidence Magic is not what it thinks itself Its source of power is faith*'

"That there are men who can do ill by evil powers like Cacodæmon I myself cannot think I cannot conceive a bel-dame inflicting harm by a look, though I know Virgil and Pliny say so Magicians we know there have been Christ's apostles beheld with wonder the works of Simon Magus Pliny asserts Nero could work magic, but more probably I think, he dabbled in poisoning It is said that today magic can put an evil spirit into a man I once was called to a youth who even seven

times a day was taken with struggling so that four servants could hardly hold him. Between whiles he was sane and knew all around him. He was thought to be possessed. In my review it was epilepsy, which is not from a demon but from the brain acting on the nerves. I ordered clysters, baths and rubbing. But if magic and the præternatural were the cause the remedy should be præternatural—prayers and offerings. But I believe today magic can at most cause the semblance of a disease. A sufferer may none the less be persuaded into thinking he truly has a disease. I have seen a paper with some writing on it strung round the neck heal such illness of the whole body in a single night. I have seen a fever banished by pronouncing a few ceremonial words. But such remedies do not cure for long. We have to be on the watch. *Illness can be fictitious, so also can cure. Human nature is perverse.*"

Here we have a glimpse of Fernel as forerunner of psychiatry and suggestion therapy. We note also how distasteful to him was empiricism.

"But Fernel was surrounded by yet another great superstition besides that of natural magic—another superstition founded on Nature, and more exalted and refined than magic. A man in those days—and in classical antiquity no less—might be sceptical about magic and yet endorse astrology. He would appraise it as a science. To Fernel's time it had come down from antiquity without loss of prestige, as a learned study of the stars. It amounted to a cult. It accredited certain aspects of the heavens with præternatural influence on man's circumstances and doings. It had its developed symbolism. It was a false mysticism which satisfied that craving for the mystical which forms a part of human nature. It demanded observances. It enjoined rites. It was taught and practised by the initiated. It was in effect a quasi-Natural Religion. We must remember that in those times cosmology was expected of religious doctrine to an extent hardly looked for from it today. If a religion can exist without bearings then astrology was a Natural Religion. It was in Fernel's time the Natural Religion of the classes and of the 'liberal minded, of the 'intelligentsia'.

"Astrology was at that time the most mathematical and probably in general opinion the most regarded branch of natural philosophy. So far as natural philosophy could claim relation and affinity to theology the 'Queen of Sciences,' the science best qualified to do so was probably in current opinion astrology.

"For Fernel, however, the stars objectively were just shining points which traced their cyclic movements round the earth with mathematical punctuality. More practised in watching them than were most, even in that age of sky-watching, he knew their risings and their settings. He had devised a special astrolabe. In his very first approaches to medicine astrology had fascinated him. He had published his book on proportion to facilitate the calculations. To know the influence of the planets, their conjunctions, their oppositions, their reinforcements and their cancelling on human health and sickness, was one of the first arts in which he practised himself after entering on medicine.

"But Fernel, despite his early enthusiasm for astrology, became, as years went by, gravely disillusioned in respect of it. His fervour for it had been prior to his entering actually on medical practice. He was at that time a mathematician and, as a young physician, reading theoretical medicine. Later had come to him first-hand care of the sick and daily charge and responsibility at the bedside. And in no ordinary measure, for his practice became very large. Then with his knowledge of the planetary sky and the starry houses and with his mathematics he was equipped, as were few, to read the astrological sooth-sayings and check them against fact. He proceeded, at first with every confidence in them, to compare what they told with what passed before his eyes in the sick room. He was not one to feel lightly his responsibilities in the sick chamber. What followed was gradual but convinced disillusion. Wholly against the current of his time he grew more and more sceptical of astrology as any true reading of the meaning either of the heavens or of disease.

"Michæl Nostradamus, the notorious astrologer, M.D., of the University of Montpellier, visited the Court. He was entrusted with horoscopes for the royal children. Fernel held aloof, and, it is said, kept the king aloof. It was the queen Catherine de Medici who rewarded Nostradamus.

"Fernel averted his face from astrology more and more. Ten years before his death he wrote: "By all means study the heavens for help to man below. The ancients did so as part of their enquiry into the nature of things. And that is right. Even as many do so today. But the astrologer is often an indifferent astronomer. There are among them some who pretend to read things in the stars which are not there. That is

an abuse of good faith They soil astronomy with superstition Some of them would bind the very freedom of the mind and of our action to the fatality of the stars There are too some who disgrace science by deliberate fraud Illness does sometimes surely derive from præternatural causes But are the planets among those causes? Rather the influences of the planets are natural forces, like the sun's light" It comes to this "Once within nature and whether the unknown come from the planets or from the elements or from animal or plant, metal or stone, it cannot help or harm except by the virtue of just some natural property The natural cannot cause the supernatural"

"Fernel was probably the greatest physician of his century Quite usually he was styled The Greatest of the Moderns We are told too of him, resourceful and somewhat severe in presence as he was, that the very note of his voice would change and soften when announcing if that were to be, that the suffered would recover" (Sherrington)

The versality and the inquiring mind of Fernel is shown by Guillaume Planey, who writes in his life of Jean Fernel, that "when consulted by some patient who was a man of parts, Fernel, if the state of the case allowed, liked to get some talk with him, if it were a philosopher on philosophy, if a mathematician on mathematics, if a commander on a soldier on the fate of towns, the rivers on which they were, and on engines of war and their inventors, if a seaman on navigation and newly discovered lands, if a theologian on God"

The revival in medicine came with William Harvey some eight years after Fernel's death when experimental method replaced empty speculation, magic and astrology But Fernel may truly be considered a forerunner of this revival, who discarded supernatural as a cause of disease, abandoned magic and astrology He relied on first hand observation of fact He impressed that on his pupils Guy Patin, of his old faculty, praising him in the following century wrote "He was a great man Our fingers have eyes, he told us and further, have the virtue that they see only what their eyes vouchsafe Myself in Christianity I believe as I should a number of things I cannot sense, that is I believe by Faith But in medicine I believe only what I see"

Original Contributions

A CLINICAL & AETIOLOGICAL STUDY OF HEART-FAILURE IN BOMBAY

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My intention, when undertaking this investigation for the first time, was to collect and study a large number of cases of cardiac failure from the files of the K E M Hospital, Bombay, extending over a period of about ten years or so, in order to gain an insight into the causes and characteristics of heart failure cases in the tropics. Though numerous statistics and papers on this subject have been published in European countries and on the continent of America, they cannot be considered truly representative of the state of affairs in India. The present study is an attempt at "filling in" this gap in our knowledge.

Because of numerous difficulties in the collection of data, e.g. inaccuracies and discrepancies in case-notes, I have had to be satisfied with a much smaller series of cases than previously meditated. The present paper deals with 600 cases of "heart failure" admitted to the hospital during the years 1938, 1939 and 1940. Over a hundred case-records had to be rejected as being "inadequate" or "inaccurate".

Objects of Study —The object of the present investigation is threefold: (1) To present the relative frequency or incidence of different aetiological factors in the genesis of heart-failure in India. (2) To present the clinical characteristics of heart failure cases in general. (3) To present the clinical and diagnostic characteristics of individual groups (based on aetiological considerations) of cases of heart-failure.

The term "heart-failure", as used in this paper, should not be confused with "circulatory failure" which includes besides "cardiac failure" peripheral failure. Cases of peripheral failure have been rigidly excluded from this series unless associated with cardiac failure.

RESULTS OF INVESTIGATION

Racial Incidence —Of the 600 cases of heart failure, 427 were Hindoos, 123 Muslims, 48 Christians and 2 Parsees. The relatively high incidence of heart-failure in a minor community (Christians) is rather

striking The low incidence of heart failure in the Parsee community is apparent and not real, considering that the rate of admission of Parsee patients at this hospital is very low In terms of percentages, 71·2 per cent were Hindoos, 20·5 per cent Muslims, 8 per cent Christians and 0·3 per cent Parsees

Sex Difference —There were 414 males, and 186 females, i.e. 69 per cent of cases were males and 31 per cent females Ratio of males to females in this series was 2·2 to 1·0 The high incidence of males is probably partly real and partly apparent,

(1) Pulmonary, Syphilitic and coronary heart diseases are much commoner in male subjects than in females In fact, my series shows a higher incidence of males in every single aetiological group of heart failure

(2) The innate diffidence on the part of Indian women to report to hospital in case of ailment, is to some extent responsible for the relatively higher incidence of heart failure in males

Age Incidence —This is extremely variable The youngest subject in the present series was 6 years old while the oldest was 89, giving a range of 83 years The average age for the whole series was calculated at 42 years There were 6 cases in the first decade of life, 51 cases in the 2nd, 111 cases in the 3rd, 177 cases in the 4th, 141 cases in the 5th, 75 cases in the 6th, 24 cases in the 7th, 12 cases in the 8th and 3 cases in the 9th decade In terms of percentages 1 per cent of cases were in the 1st decade, 8·5 per cent in the 2nd, 18·5 per cent in the 3rd, 29·5 per cent in the 4th, 23·5 per cent in the 5th, 12·5 per cent in the 6th, 4 per cent in the 7th, 2 per cent in the 8th and 0·5 per cent in the 9th decade It will be observed that the highest incidence of failure cases was in the 4th and 5th decades of life

Duration of Symptoms of Failure before Admission —The average duration of symptoms of failure before admission to hospital was 5 months, the range being very wide, from "several hours" to 10 years The great majority of cases admitted to hospital were admitted within a year of onset of failure symptoms

PRESENTING SYMPTOMS

Dyspnoea or shortness of breath was a presenting symptom in 65 per cent of cases, oedema or anasarca in 40 per cent, cough in 39 per cent, "distended abdomen" in 13 per cent, abdominal pain in 11 per cent paroxysmal dyspnoea or "cardiac asthma" in 9 per cent, weakness, lassitude or undue fatigue in 5 per cent, palpitation in 4 per cent vertigo in 3 per cent, chest pain in 2·5 per cent, fainting in 2·3 per cent drowsiness in 1·6 per cent, insomnia in 1·5 per cent, excessive uterine bleeding in 1 per cent and diminished output of urine in 0·7 per cent

Enumeration of Symptoms—Table I gives a list of all symptoms met with, in order of importance. About 32 symptoms are listed in the table.

Table I Subjective manifestations of Cardiac Failure in order of importance (Percentage frequencies)

Symptom	%	Symptom	%
1 Dyspnoea	93	17 Parasthesiae	4
2 Oedema	88	18 Joint Pains	3
3 Cough	89	19 Restlessness	3
4 Ascitis	59	20 Hiccough	3
5 Abdominal Pain	23	21 Haemoptysis	2.3
6 Lassitude or debility	16	22 Ictericæ	2
7 Flatulence	15	23 Headache	2
8 Chest Pain	9	24 Menorrhagia	1.6
9 Fever	9	25 Thirst	1.3
10 Oliguria	7.3	26 Dysphagia	1.3
11 Vertigo (giddiness)	7	27 Numbness	1.3
12 Diarrhoea	6	28 Hoarse voice	1.3
13 Anorexia	6	29 Rectal Bleeding	1
14 Palpitation	5	30 Amenorrhoea	1
15 Bodyache	5	31 "Brassy cough"	1
16 Constipation	5	32 Drowsiness	0.7

Dyspnoea or Shortness of breath comes first with an incidence rate of 93 per cent. For the sake of precision I have further analysed the symptom of dyspnoea into five main types, (1) Exertional dyspnoea or dyspnoea of exertion. This was noted in 89 per cent of cases (2) continuous dyspnoea in 65 per cent of cases (3) Paroxysmal dyspnoea or cardiac asthma in 16 per cent of cases (4) Orthopnoea in 31 per cent of cases (5) In 2 cases (i.e. 0.3 per cent), dyspnoea was noted only in the sitting up posture and relieved by lying down.

All cases of "continuous dyspnoea" also suffered from "exertional dyspnoea". In only 7.5 per cent of cases of continuous dyspnoea were there associated paroxysms of cardiac asthma. It is interesting to note that in 7 per cent of cases of "heart failure" there is no complaint of dyspnoea.

Oedema as a symptom, rates second to dyspnoea in order of importance, being noted in 88 per cent of cases. Oedema was confined to the lower extremities (ankles or legs) in 472 cases, (79 per cent of all cases). Oedema of the upper extremities or hands was noted in 8 per cent of cases only (45 cases), it was noted in the absence of oedema of the lower extremities in only 11 cases (2 per cent). In 24 cases (4 per cent), oedema of the upper extremities was associated with oedema of the face. In 16 cases (2.7 per cent), oedema was noted in one upper extremity only, it was right-sided in 10 cases and left-sided in 6. Oedema of the face was noted in 144 cases (24 per cent) of these only 19 cases (3 per cent), lacked oedema of the lower extremities. In 3 cases (0.5 per cent), oedema was confined to the neck only. Oedema of the abdominal wall was mentioned in only 2 per cent (12 cases) of case Records, obviously an underestimate. Generalized anasarca was noted in 27 per cent of cases (16 cases).

Cough ranks third in order of importance, being noted in 59 per cent of cases, 45 per cent of cases had "cough with expectoration", with oedema of the face. In 16 cases (27 per cent), oedema was more than three times as common as dry cough.

Abdominal pain was noted in 23 per cent of cases, that is, one case in every four of heart failure complains of pain in the abdomen. In 55 cases (93 per cent) pain was noted in the "right hypochondrium", in 5 cases (9 per cent) in the "left hypochondrium", in 8 cases (11 per cent) in the epigastric region, in 2 cases (3 per cent) in the hypogastric region and in 68 cases (113 per cent) it was generalized. The high incidence of pain in the right hypochondrium is probably due to liver congestion.

Weakness, lassitude or excessive fatigue was noted in 16 per cent of cases, it comes sixth on the list of symptoms. This is obviously an underestimate. In private practice, direct questioning of cardiac patients discloses this symptom to be an almost constant and probably the earliest feature of a "failing heart". Its low incidence in hospital patients is apparent only, due partly to inadequate "history-taking" and partly to the relatively "benign nature" of this symptom from the point of view of the hospital patient.

Chest pain was encountered in 9 per cent of cases only. The low incidence of pain in the chest in cases of heart failure is striking. It will be observed that abdominal pain was about three times as common as chest pain. There is a much higher incidence of chest pain in private cases of heart failure.

Palpitation was met with in 5 per cent of cases only. One is struck by the low incidence of this symptom in hospital cases, considering its great frequency in private practice.

A review of the symptoms in cases of heart failure will disclose the high incidence of symptoms referred to the gastrointestinal tract e.g. abdominal pain, flatulence, constipation, diarrhoea, anorexia, thirst, hiccough, dysphagia and bleeding per rectum.

Heart Size —There are 3 main ways of determining the size of the heart (1) by determining the site of the apex beat (inspection or palpation) (2) By percussing the cardiac borders and (3) by X-Ray projection (orthodiagraphy or Teloradiography). It is generally recognized, nowadays that the radiographic method of determination of heart-size constitutes a distinct advance on the old methods of palpation and percussion, unfortunately, as the roentgenographic method is not employed in hospital as a routine measure in cases of this type, I have had to rely on the less accurate and simpler methods of gauging heart size. Many physicians of note place little or no credence in these methods of determining the size of the heart, it is true that these methods fail to give reliable data in the hands of the unexperienced but with practice they certainly gain precision.

I have classified heart-failure cases into 6 groups according to the size of the heart (See Table 2)

TABLE 2 SIZE OF THE HEART

	%
1 Smaller than normal	33
2 Normal in size	21
3 Slight enlargement	31
4 Moderate enlargement	18
5 Great enlargement	16.3
6 Size doubtful	8.3

For the purposes of this classification, certain arbitrary limits had to be fixed. By "slight enlargement" is meant an apex beat on left cardiac border in the 5th interspace more than $3\frac{1}{2}$ inches and less than $4\frac{1}{2}$ inches from the mid-line, "moderate enlargement" means that the apex beat on left cardiac border is from $4\frac{1}{2}$ inches to $5\frac{1}{2}$ inches in the 5th space or from $3\frac{1}{2}$ inches to $4\frac{1}{2}$ inches in the 6th space, any heart size exceeding these limits is classed as "great enlargement." Enlargement of the right side of the heart (as shown by outward displacement of the right cardiac border) is considered separately.

It will be observed from Table II that in 50 cases (8.3 per cent.), the size of the heart could not be determined. The majority of such cases belong to the group of Emphysema Heart, the apex beat in such cases was neither visible nor palpable while percussion was incapable of mapping out the borders of the heart. In over 24 per cent of cases (about one case in every four), the size of the heart was within normal limits. In spite of definite evidence of heart failure, the heart showed no increase in size in these cases. It is possible that in some of these cases, the heart may be unduly small to begin with (the so-called "vertical heart" or "drop heart"), as a result, the earlier phases of cardiac enlargement are missed.

Heart Murmurs — (See Table 3) Heart Murmurs were described in 271 cases (45 per cent of cases) only. In 329 cases (55 per cent) there were no murmurs described, an interesting finding considering the importance allotted to murmurs by teachers and text-books of medicine.

TABLE 3 HEART MURMURS

		%	
Incidence of murmurs		45	
" " systolic murmurs		36	
" " diastolic murmurs		15.7	
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Systolic	%	Diastolic	%
Generalized or precordial	23	Mitral	61
Mitral or apical	54	Aortic	12
Pulmonary	9	3rd space	16.8
Third left inter-space	3	Multiple	6.4
Aortic area	9		
Mitral and aortic areas	2		

Systolic murmurs were noted twice as frequently as diastolic murmurs, the percentage incidence in the two cases being 36 per cent and 15.7 per cent respectively. The low incidence of pulmonary systolic murmurs in this series is striking. In the great majority of cases, systolic murmurs were noted either in the mitral area or all over the precordium.

Diastolic murmurs were encountered in the mitral areas much more often than in the aortic area (about five times as common). The incidence of diastolic murmurs was higher in "the third left inter-space" than at the aortic area.

Character of the Apex Beat—This was described as "normal" in 236 cases (30.3 per cent), as "weak" or "feeble" in 223 cases (37.3 per cent), as "not palpable" in 95 cases (15.7 per cent) and as "heaving" or "forcible" in 46 cases (7.7 per cent).

General Appearance of Patient—*Pallor* of the skin and mucous membranes was noted in 37.3 per cent of cases (223 cases). In 1 per cent (6 cases) the appearance was described as "plethoric." *Cyanosis* was observed in 11.7 per cent of cases only (70 cases), it is interesting to note that in as many as 88.3 per cent of cases of heart failure, no mention was made of cyanosis. An *icteric* tinge was noted in 2.7 per cent of cases (16 cases).

Clubbing of nails was observed in 11 per cent of cases (65 cases).

Venous Phenomena—Engorgement of neck-veins was observed in 65.7 per cent of cases (394 cases); in 113 cases (19 per cent) it was noted as "slight" and in 281 cases (46.7 per cent) as "severe." This sign of failure" was reported absent in 34.3 per cent of cases.

Pulsation of neck-veins was observed in 31.4 per cent of cases only (189 cases).

It will be observed that while venous engorgement was noted in 65.7 per cent of cases, venous pulsation was noted in only 31.4 per cent.

Liver, Spleen and Ascitis—In 30.3 per cent of cases (181 cases) no enlargement of the liver was observed. The liver was noted as "enlarged" in 69.7 per cent of cases, in 16.4 per cent (99 cases) the enlargement was "slight", in 37.0 per cent (223 cases) it was "moderate" and in 16.3 per cent (97 cases) it was "great".

The liver was described as "tender" to palpation in 66.7 per cent of cases (402 cases), in 34.7 per cent (210 cases) tenderness was "slight" while in 32.0 per cent (192 cases) it was "marked".

The liver failed to show tenderness or enlargement in approximately one-third of the cases investigated.

Enlargement of the spleen is not a feature of cardiac failure according to most cardiologists. In the present series of cases, en-

enlargement of the spleen or splenomegaly was observed in 13.6 per cent of cases, in 6.3 per cent (39 cases), the enlargement was "slight", while in 7.3 per cent (44 cases) it was "great". In other words, splenic enlargement was noted in about one case in every seven of heart-failure. It is possible that in some of the cases, the splenomegaly might have been due to some associated tropical disease like chronic malaria, there were many cases, where the cause of enlargement of the spleen remained obscure. Personally, I am convinced that splenic enlargement may arise in cases of heart-failure as a "congestive phenomena", as in the case of the liver.

Pyrexia —In 79 per cent of failure cases (473 cases) the course pursued was "afebrile", the average temperature being about 97° F. The maintenance of a subnormal temperature in these cases was striking. 21 per cent of cases (127 cases) were febrile the temperature ranging from 96.9° F to 104° F.

The Pulse —The pulse rate on admission was extremely variable ranging from 52 to 165 beats per minute. In a small percentage of cases, the pulse rate was actually below normal levels. The average pulse rate on admission was calculated as 102 per minute, for the whole series. The pulse was reported as "weak", "feeble" or "difficult to feel" in the majority of cases. The pulse was described as "irregular" in 10 cases (18.3 per cent). In four out of every five cases of failure the pulse was regular. Auricular fibrillation was observed in 6 per cent of cases (36 cases) while extrasystoles were noted in 11.5 per cent of cases (69 cases).

The pulse was described as "water-hammer", "collapsing" or "Corrigan" in 12.7 per cent of cases (77 cases), the great majority of these cases were secondary to either aortic regurgitation or anaemia.

Respiration Rate —The respiration rate was found to vary from 16 to 60 per minute, the average for the whole series being about 28 per minute.

Blood Pressure —Blood pressure readings were extremely variable in the present series of cases. The systolic blood pressure varied from 85 to 230 mm Hg. The average systolic pressure for the series was 108 mm Hg. The diastolic blood pressure varied from 20 mm Hg to 150 mm Hg, with an average of 65 mm Hg. The pulse pressure or differential pressure varied from 20 mm Hg to 170 mm Hg, with an average of 45 mm Hg. The unbelievable pulse pressure of 170 mm Hg was observed in a case of Aortic Regurgitation.

Pulmonary Congestion —In 38.3 per cent of cases (229 cases) there was no evidence of pulmonary congestion. Crepitations or moist sounds (indicating congestion) were observed in 61.7 per cent of cases (371 cases). In 198 cases, the crepitations were "basal", in 168 cases "diffuse" or "generalized" and in 5 cases, "apical". In 323 cases, crepitations were bilateral, in 35 cases confined to the left side of the chest and in 13 cases confined to the right side of the chest.

In cases of unilateral distribution, crepitations were observed on the left side almost three times as often as on the right side.

This confirms my previously expressed view about failure cases viz "in cases of heart failure, fluid in the pleural cavity (hydrothorax) shows a predilection for the right side, while fluid in the lung-tissue (crepitations) shows a predilection for the left side", this has been borne out by a study of failure cases, in both private and hospital practice

Signs of consolidation of lung-tissue, with patchy dullness or percussion and bronchial breathing, were observed in 17 per cent of cases only (10 cases)

Blood Reaction for Syphilis —A "positive" Wassermann or Kahn reaction for Syphilis was reported in 16 per cent of cases (97 cases) This figure is obviously inaccurate, since syphilis was looked for in a percentage of cases only

The Urine —(1) The specific gravity of urine was found to vary from 1005 to 1030, the average being 1019 (2) Albumin was reported "present" in 281 cases (47 per cent), in 152 cases, in "small amounts" and in 129 cases in "large amounts" In 53 per cent of cases (319 cases) there was no albumin in the urine (3) Sugar in the urine was detected in 3 per cent of cases (18 cases) (4) Granular casts were noted in 17 per cent (43 cases) and triple phosphate crystals in 20.7 per cent (94 cases) of cases, in 56 cases, "in small numbers" and in 36 cases "in large numbers" (6) Red blood cells were present in 7 per cent (42 cases) (7) Crystals Calcium oxalate crystals were noted in 7.2 per cent (43 cases) and triple phosphate crystals in 20.7 per cent (124 cases) (8) Bile salts and pigments were detected in 1.3 per cent cases (8 cases)

Blood Count —This was determined in a fair percentage of cases The red cell count was found to vary from 0.7 to 4.9 millions per c m m with an average of 3 million The haemoglobin percentage varied from 15 per cent to 90 per cent with an average of 58 per cent The Colour index varied from 0.60 to 1.30 with an average of 0.90

The white cell count varied from 2,000 to 22,175 per c m m with an average of 8,200 per c m m The differential counts showed, Polymorphonuclear cells from 34 to 90 per cent with an average of 65 per cent, lymphocytes from 2 to 42 per cent with an average of 29 per cent, Eosinophils from 0 to 50 per cent, with an average of 3.4 per cent, large mononuclear ranging from 0 to 8 per cent with an average of 2.8 per cent The Eosinophil cells showed very high counts in some cases, especially in cases of pulmonary origin

Duration of Stay in Hospital —The stay in hospital varied from 10 minutes to 8 months in the 600 cases, with an average of 17 days

The "stay" in fatal cases, varied from 10 minutes to 8 months with an average of 11 days, in cases that recovered, the stay ranged from 1 day to 6 months, with an average of 23 days

Recovery Rate —Of the 600 cases of failure, 357 recovered (59.7 per cent) and 243 cases (40.3 per cent) proved fatal

THE AETIOLOGY OF HEART FAILURE

The aetiological factor or factors, responsible for heart-failure could be determined in 526 cases (87.7 per cent) of the present series. In the remaining 74 cases (12.3 per cent) the aetiology remained "obscure" or "doubtful"

TABLE 4 THE AETIOLOGY OF HEART-FAILURE
(Aetiological Groups)

	%
1 'Pulmonary group' (i.e. secondary to lung diseases)	30
2 Valvular Heart Disease	25.5
3 Anaemias (various forms)	13.2
4 Hypertensive heart disease	6.8
5 Coronary sclerosis or myocardial degeneration	6.3
6 Vitamin B Deficiency	1.7
7 Thyrotoxicosis	1.0
8 Pericardial diseases	1.2
9 Congenital heart disease	0.7
10 Aortic aneurysm	0.7
11 Malignant endocarditis	0.5
12 Rheumatoid arthritis	0.3
13 Aetiological factor obscure	12.3

Aetiological factors concerned in the genesis of heart-failure are presented in tabular form, in order of importance, in Table IV. A perusal of this will bring certain interesting facts to light —

(1) The importance of lung-disease as a cause of heart-failure. Practically a third of the cases of failure (30 per cent) owe their origin to one or other disease of the lung. The importance of this factor is not dealt with adequately in text-books of medicine. For the sake of convenience, this group of cases has been labelled "the pulmonary group" of failures.

(2) Valvular diseases of the heart account for only a quarter of the cases of heart-failure (25.5 per cent).

In other words, 75 per cent of failures are non-valvular in origin. In the teaching of medicine to students, too much stress has been laid on valvular diseases of the heart at the expense of non-valvular disorders. Much has been written and said about murmurs and lesions of the valves while emphysema, asthma, bronchitis etc., are seldom mentioned as causes of failure. The present series of cases serves to emphasize the importance of non-valvular heart-failure.

(3) Anaemias account for about one-eighth of all cases.

(4) High blood pressure accounts for only 6.8 per cent of cases. This may be so for hospital patients but is certainly a gross underestimate for private cases, where hypertension plays a considerable role in the causation of heart-failure.

(5) "Coronary sclerosis" is seldom diagnosed correctly. In the great majority of cases, it is labelled "Myocardial degeneration". 38 cases of the present series could be allotted to this group, after detailed study.

(6) Vitamin B Deficiency was responsible for only 10 cases (i.e. 1.7 per cent) of the present series.

In many cases of failure the diagnosis of Beri-beri heart is not entertained by the average physician, who is totally unfamiliar with the clinical picture of this "not-too-uncommon" disease. There is no doubt that with growing knowledge of its existence and with greater help from the laboratory, the condition of Beri-beri Heart will assume a more important role in the aetiology of heart-failure.

(7) The low incidence of Thyrotoxic heart failure (1 per cent) is striking.

A Study of individual groups of Heart-failure cases—Each group of heart failure cases (according to the aetiological classification set fourth in Table 4) was studied for individual peculiarities and diagnostic criteria. The main findings of this investigation are set out in Table 6.

TABLE 5 "THE PULMONARY GROUP" OF FAILURE

	Case numbers
Total number of cases	179
Chronic Bronchitis	68
Asthma	52
Emphysema	11
Pneumonia	6
Pulmonary tuberculosis	5
Bronchiectasis	3
Pleural Effusion	4

THE PULMONARY GROUP—(See Table 5). This includes cases of heart-failure secondary to diseases of the lung. 30 per cent of failure cases (179 cases) belong to this group. The pulmonary group of diseases ranks first in the causation of heart-failure. It will be observed from Table 5 that asthma, emphysema and chronic bronchitis are together responsible for 90 per cent of case of the pulmonary group, the term 'asthma-emphysema-bronchitis group' is used to include these three diseases which occur either singly or in combination and which play such an important role in the causation of heart-failure.

Table 6 Clinical Manifestations of Individual Aetiological groups of Failure cases

		Pulmonary group	Myocardial group	Mitral group	Aortic group	Hypertensive group	Coronary Sclerosis	Vit B Deficiency	Whole Series
Number of Cases		170	79	102	44	41	38	10	600
Percentage of Total		30%	13.2%	16.6%	7.3%	6.8%	6.3%	1.7%	100%
Ratio of male to females		5.5	1.7	1.3	6.3	1.3	1.6	1.5	2.2
Duration (in months)		5	1.5	3	9	1.5	5	2	5
% Incidence of Symptoms	Dyspnoea	45%	55%	98%	88%	72%	90%	80%	65%
	Oedema	15%	50%	58%	23%	45%	16%	100%	40%
	Cough	60%	25%	13%	28%	10%	11%		39%
	Abdominal Pain	1%	15%	10%	5%		22%	20%	11%
	Chest Pain		5%	5%	10%	10%	12%		3%
	Palpitation		20%	13%			11%		1%
	Vertigo		25%			25%			3%
Heart Size	Normal	18.7%	12.5%	10%	14%	10%	16%	60%	24%
	Slight Enlargement	33.5%	37.5%	30%	19%	25%	15%	10%	31%
	Moderate Enlargement								
	Gross Enlargement								
Murmur	Incidence	12.5%	35%	100%	100%	44%	11%	10%	45%
	Systolic	12.5%	35%	81%	62%	44%	11%	10%	36%
	Diastolic			52%	77%				15.7%
General appearance	Pallor	25%	100%	30%	36%	20%	34%	60%	37.3%
	Cyanosis	22%	2.5%	20%	14%	10%	6%		12%
	Clubbing	32%	2.5%	20%	5%		11%		11%
	Icterus	2%		1%	5%				2.7%
Tender Liver		80%	15%	53%	68%	70%	71%	30%	67%
Enlargement of Liver		80%	50%	88%	86%	70%	36%	40%	70%
Enlargement of Spleen		7%	20%	20%	19%	5%	11%	10%	11%
Ascites		60%	15%	10%	37%	10%	11%	60%	38%
Neck Veins	Engorgement	98%	11%	84%	64%	15%	16%		66%
	Pulsation	62%	23%	51%	25%	10%	34%		31%
Oedema	Face	15%	15%	33%		55%	23%	60%	21%
	Arms	20%	30%	25%		20%	6%		8%
	Legs	90%	80%	85%		90%	59%	100%	79%
Pulse	Rate	93	108	103	123	88	103	100	162
	'Water Hammer'		21%		100%				
	Extrasystoles	10%	5%	16%	9%	35%			11.5%
	Fibrillation	1.3%		1%					6%
Respiration Rate		27	31	26	27	26	28	27	28
Blood Pressure	Systolic	112	111	99	134	183	116	108	108
	Diastolic	68	70	72	35	112	78	68	65
	Pulse Pressure	42	41	26	102	71	38	42	45
Incidence of Syphilis		22.5%	5%	3%	48%	1%	6%		16%

THE ASTHMA-EMPHYSEMA-BRONCHITIS GROUP — Total number of cases in this group was 161 (26.8 per cent of the whole series)

Sex Differences — There were 136 males and 25 females giving a ratio of males to females of 5.5 to 1.0. The high incidence of males in this group is striking. Of the 25 female subjects in the "asthma-emphysema-bronchitis group", 18 had chronic bronchitis, 4 had asthma and only 3 had emphysema. (When two or more of these conditions co-exist in any given case, then the primary aetiological factor is determined for the purposes of analysis, for example, if in a patient with asthma, emphysema and bronchitis, the primary disease is asthma, then the case is regarded as one of asthma.) Of the 136 males in this group, 50 had chronic bronchitis, 37 had emphysema and 49 had asthma.

13.5 per cent of females in this series belong to the "asthma-emphysema-bronchitis group," while of males 33 per cent belong to this group. Besides the relative preponderance of males in this group another feature worthy of note is the higher incidence of bronchitis in females and of emphysema and asthma in males.

Age Distribution — Patients ranged in age from 20 to 80 years, the average being 44 years. The average age for males was 45 years and for females, 39 years, giving a difference of 6 years between the averages. There were 4 subjects in the 2nd decade, 12 in the 3rd, 51 in the 4th, 56 in the 5th, 22 in the 6th, 12 in the 7th, and 4 in the 8th decade of life.

Duration of Symptoms before admission — The term "Duration of Symptoms" may mean either "duration of symptoms of the causative disease" or "duration of symptoms of heart failure."

(1) With regard to the *causative disease*, the average duration of the symptoms for this group was 5 years, for chronic bronchitis alone it was 4½ years, for asthma 6¼ years and for emphysema 5 years. The shortest duration was 1 month and the longest 20 years.

(2) As regards *symptoms of heart-failure*, the average duration of symptoms for the group was 6 months, the average for bronchitis was 7½ months, for asthma 3 months and for emphysema 6¼ months. The minimum duration was 4 days and the maximum 5 years.

Heart failure supervenes on chronic bronchitis on an average about 4 years after the onset of the disease, in the case of asthma the average is 6 years and for emphysema 4½ years.

From the above one observes that in spite of failure supervening either in bronchitis than in emphysema and earlier in emphysema than in asthma, once the failure has started, its cause is more rapid in asthma than in emphysema and in emphysema than in bronchitis.

In other words, heart failure though appearing later in asthma, is more rapidly progressive in this disease than in the other members of the "pulmonary group"

Presenting Symptoms —Dyspnoea or shortness of breath was a presenting symptom in 45 per cent of cases (73 cases), cough in 60 per cent (95 cases), oedema in 15 per cent (24 cases), distension of the abdomen in 2 per cent (4 cases) and abdominal pain in 1 per cent (2 cases). Interesting features to note are —

(1) The importance of cough as a presenting symptom, it tops the list of symptoms (2) Dyspnoea is observed in less than half of the cases (3) Oedema is noted in only 15 per cent of cases (4) Chest pain and palpitation are not reported in this group as first or primary symptoms

Heart Size —In 15 per cent of cases (24 cases) the size of the heart was described as "normal," in 3.7 per cent (6 cases) as "smaller than normal," in 33.5 per cent (53 cases) as "slightly enlarged," in 14.8 per cent (23 cases) as "moderately enlarged," in 13 per cent (21 cases) as "greatly enlarged" while in 21 per cent (34 cases) it was "difficult to determine." Owing to the high incidence of emphysema in this group, considerable difficulty was experienced in the determination of heart size. In no other group of failure cases did we find such a high incidence of normal reports with regard to heart size. It will be observed from the above data that cardiac dilatation in cases of pulmonary heart failure is usually of "slight" degree.

Right-sided enlargement of the heart was observed in only 3.2 per cent (5 cases) of cases of this group.

Heart Murmurs —A murmur was observed in 12.5 per cent of cases only (20 cases), the low incidence of murmurs in this group is striking. In all cases, murmurs reported were "Systolic", diastolic murmurs being unknown to this group. In 4 cases, the murmur was "generalized or precordial" while in the remaining 16, it was localized to the mitral or apical area. In 18 cases, the murmur was "soft and blowing" in character while in 2 it was described as "rough and grating." Conduction to the axilla was noted in 2 cases only. The site of maximum localisation of the murmur was the mitral area in all cases.

General Appearance —*Pallor* of the skin and mucosa was described in 25 per cent of cases, *Cyanosis* in 22 per cent, and *icterus* in 2 per cent. *Clubbing* was noted in 32 per cent of cases. The high incidence of clubbing is striking. In no other type of failure was such a high percentage incidence noted.

Neck Veins Engorgement of the neck veins was noted in as many as 98 per cent of the cases. It was observed in only 66 per cent of the whole series of 600 cases. Pulsation of veins was noted in 62 per cent of cases, (noted in 31 per cent of all cases).

Liver, Spleen and Ascitis—The liver was not tender in 20 per cent of cases (32 cases), it was "slightly" tender in 55 per cent (87 cases) and "markedly" tender in 25 per cent (42 cases). In 20 per cent of cases (32 cases) there was no enlargement of the liver, in 25 per cent (39 cases) there was "slight" enlargement, in 35 per cent (56 cases) "moderate" enlargement and in 20 per cent (33 cases) "great" enlargement. In other words, four out of every five cases in this group showed tenderness and enlargement of the liver. Spleen enlargement was observed in 7 per cent of cases (11 cases) only. In 93 per cent, it was not palpable. Free fluid was detected in the abdomen in 60 per cent of cases (96 cases), in 50 per cent (82 cases) it was "small" while in 10 per cent (16 cases) it was "mattive". **Oedema**—The distribution of oedema was studied in this group. In 10 per cent of cases (16 cases), there was no oedema, in 40 per cent (63 cases), oedema was confined to the lower extremities, in 25 per cent (42 cases) it was noted in the lower extremities and face, in 10 per cent (16 cases) in the lower and upper extremities and face, in 15 per cent (24 cases) in the face, upper and lower extremities. Oedema of the lower extremities was noted in 90 per cent, of the upper extremities in 25 per cent and of the face in 40 per cent. In only 3 cases did oedema of the face precede oedema of the lower extremities in none of these cases was there evidence of kidney disease.

The Pulse—The pulse rate on admission varied from 52 to 125 in the 16 cases, the average being 93 per minute. Considering that the average pulse rate for the whole series is 102, the average for this group is rather low. In 10 cases, the pulse rate, in spite of heart failure, was below 75 per minute. The pulse was described as "irregular" in 18 cases (11.3 per cent), in 16 cases (10 per cent) the irregularity was accounted for by extrasystoles while in 2 cases (1.3 per cent) there was auricular fibrillation. A "collapsing" pulse was noted in 6 cases (3.8 per cent) in spite of there being no associated incompetence of the aortic valve.

Respiration Rate—This varied from 19 to 45 per minute with an average of 27 per minute.

Blood Pressure—The systolic pressure in this group ranged from 85 to 180 mm Hg, with an average of 112 mm Hg. The diastolic pressure ranged from 50 to 100 mm Hg with an average of 68 mm Hg. The pulse pressure ranged from 20 to 120 mm Hg, with an average of 42 mm Hg. In only one case did the pulse pressure exceed 60 mm Hg (value of 120 mm Hg).

Blood Reaction for Syphilis—A +ve reaction for syphilis was reported in 22.5 per cent of cases of this group. Chronic bronchitis gave +ve reaction in 18 per cent of cases, asthma in 12 per cent and emphysema in 45 per cent. The strikingly high incidence of a +ve reaction in emphysema cases suggests a possible aetiological role for syphilis in the causation of emphysema. A large-scale study of

emphysema cases is increasingly in order to determine the role of syphilis, if any, in the causation

Blood Count —The red cell count ranged from 1.1 to 5.1 millions with an average of 3.8 millions, the Haemoglobin ranged from 15 per cent to 88 per cent with an average of 64 per cent, the colour index ranged from 0.70 to 1.10 with an average of 0.96. The white cell count ranged from 5,200 to 14,800 cells per cmm, the average being 8,600 cells.

The percentage of polymorphs ranged from 33 to 90 per cent with an average of 65.5 per cent, lymphocytes ranged from 2 per cent to 56 per cent with an average of 25.5 per cent, Eosinophils ranged from 0 per cent to 50 per cent with an average of 8.4 per cent, mononucleals ranged from 0 per cent to 3 per cent of 8.4 per cent mononucleals ranged from 0 per cent to 3 per cent. absence of erythrocytosis or polycythaemia (2) the comparatively high colour index (0.96), (3) high eosinophil counts (average 8.4 per cent), in 48 per cent of cases, the eosinophil count exceeded the value of 5 per cent.

Duration of Stay in Hospital —The duration of stay in hospital varied from 2 hours to 2 months in the "pulmonary group", the average being 13 days. In fatal cases, the stay varied from 2 hours to 1½ months, the average being 8½ days, in cases that recovered the average stay was 18 days, the range being 1 day to 2 months.

Recovery Rate —Of the 161 cases, 97 cases (60 per cent) recovered and 64 cases (40 per cent) proved fatal.

THE ANAEMIA GROUP —There were 79 cases in this group (13.2 per cent of the whole series).

Forms of Anaemia —Owing to an inadequacy of case reports an efficient aetiological classification is not possible. The cases fall into the following four classes: (1) Low colour index anaemias, 28 cases (35 per cent), (2) High colour index anaemias, 26 cases (32.5 per cent), (3) Normal colour index anaemias, 19 cases (25 per cent), (4) Cases secondary to malaria, 6 cases (7.5 per cent).

Sex Differences —There were 50 males and 29 females giving a ratio of males to females of 5, 3. The high incidence of females in this group was striking. The high incidence of anaemia in Indian women is too well known to need reiteration.

In the "low colour index" group of anaemia (microcytic) there were 18 males and 10 females, (ratio of 1.8 : 1.0). In the "high colour index" group (macrocytic), there were 18 males and 8 females (2.3 : 1.0). In the "normal colour index" group (normocytic) there were 12 males and 7 females (1.7 : 1.0). In the malarial group, there were 2 males and 4 females (0.5 : 1.0). There was a preponderance of

males in the "high colour index" group and a preponderance of females in the material group. The other groups occupy an intermediate position.

Age Distribution —Patients varied in age from 10 to 70 years, the average for the group being 38 years. In the case of Microcytic or low colour index anaemia, cases ranged in age from 11 to 50 years, the average being 31 years. With Macrocytic or high colour index anaemia, the range was 25 to 60 years and the average 42 years. With Normocytic or normal colour index anaemia the range was 10 to 70 years, and the average 46 years. Malarial cases ranged in age from 25 to 40 years, the average being 32 years.

Duration of Symptoms before admission —The average duration of symptoms of failure before admission was $4\frac{1}{2}$ months, it varied from 1 day to 3 years.

Presenting Symptoms —Dyspnoea or shortness of breath was a presenting symptom in 50 per cent of cases, Oedema in 50 per cent, debility or weakness in 32.5 per cent, cough in 25 per cent, vertigo in 25 per cent, palpitation in 20 per cent, abdominal pain in 15 per cent, anorexia or thirst in 5 per cent, vomiting in 5 per cent, drowsiness in 2.5 per cent, fever in 2.5 per cent and excessive sweating in 2.5 per cent.

Feature to note are (1) Shortness of breath in less than half of the cases, (2) the relative importance of debility and vertigo as symptoms in this group, (3) Palpitation was observed as an early symptom more often in this group than in any other, with the exception of the Thyrotoxic group.

Heart Size —In 7.5 per cent of cases (6 cases) the size of the heart was described as "smaller than normal", in 35 per cent (27 cases) as "normal in size", in 37.5 (30 cases) as "slightly enlarged", in 10 per cent (8 cases) as "moderately enlarged" and in 5 per cent (4 cases) as "greatly enlarged", in 5 per cent (4 cases) of cases the heart-size could not be determined. Right sided enlargement was observed in 2.5 per cent (2 cases) only.

Note (1) the low incidence of "large hearts" in anaemia, (2) in almost 80 per cent of cases, the heart size was within normal limits or only slightly enlarged, (3) right-sided enlargement was unusual in this group.

Heart Sounds —The *first sound* of the heart was described as 'normal' in 40 per cent of cases (31 cases), as "feeble" in 40 per cent (32 cases), as "hardly audible" or "inaudible" in 15 per cent (12 cases) and as "accentuated" in 5 per cent (4 cases). The *second sound* was normal in 55 per cent (43 cases), "feeble" in 17.5 per cent (13 cases), "hardly audible" or "inaudible" in 12.5 per cent (11 cases) and "accentuated" in 15 per cent (12 cases).

Age Distribution —Patients ranged in age from 12 to 75 years in this group with an average of 32 years. In the "mitral group", the range was 12 to 50 years, the average age being 28 years. In the "aortic group", the range was 20 to 75 years, and the average 41 years. The average age was 13 years lower in the mitral group than in the aortic group, probably accounted for by the higher incidence of rheumatism in the mitral group and of syphilis in the aortic group. In the "mitral and aortic group", the range was 25 to 30 years, the average being 27 years.

The average age for males in the "valvular group" was 35 years and for females 28 years. The difference is probably accounted for by the higher incidence of females in the "mitral group".

THE "MITRAL GROUP" —There were 102 cases in this group (17 per cent of the series).

Duration of Symptoms before admission —The average duration of symptoms of failure before admission, was 3.1 months, duration varied from 2 days to 2 years. In 40 per cent of cases of mitral disease, the duration of symptoms before admission was less than one month and in only 10 per cent was to over one year. In other words heart failure, once it starts in mitral disease, tends to pursue a rapid course.

Presenting Symptoms —Dyspnoea was a presenting symptom in 98 per cent of cases, Oedema in 58 per cent, cough in 43 per cent, palpitation in 13 per cent, debility or weakness in 13 per cent, abdominal pain in 10 per cent, abdominal distension in 10 per cent, oliguria in 8 per cent, chest pain in 5 per cent, body-ache in 5 per cent, restlessness in 5 per cent, "indigestion" in 5 per cent and haemoptysis in 3 per cent. Features worthy of note are (1) the high incidence of dyspnoea and (2) the relatively high incidence of palpitation.

Heart Size —In 10 per cent of cases, the heart size was described as "normal", in 30 per cent, it showed "slight enlargement" in 20 per cent, "moderate" enlargement and in 40 per cent "great" enlargement. Enlargement of the heart was noted in 90 per cent of cases. A study of these figures reveals the interesting fact that in mitral disease, cardiac enlargement, once it starts, progresses rapidly from "slight" to "great", the incidence of "moderately" enlarged hearts being low. Enlargement of the heart to the right was observed in 32 per cent of cases, with the exception of Beri-beri heart, mitral disease ranks first as cause of right-sided enlargement of the heart.

Considerable displacement of the apex beat was noted in some cases of mitral disease. In one case it was situated in the 7th space, 6 inches from the midline, and in another in the 7th space beyond the anterior axillary line.

Heart Sounds —The first sound was "normal" in 50 per cent of cases, "accentuated" or "banging" in 40 per cent, "feeble" in 2.5 per cent and "replaced by murmur" in 7.5 per cent.

The *second sound*, was "normal" in 25 per cent and "accentuated" (with or without reduplication) in 75 per cent

The great tendency for "accentuation" of the second sound in cases of mitral disease should be noted

Heart Murmurs—Murmurs were observed in all cases of mitral disease. Systolic murmurs were described in 82 cases (87 per cent) and diastolic murmurs in 52 cases (52 per cent)

Systolic Murmurs—Of the 82 cases with systolic murmurs, 50 had systolic murmurs alone while 32 cases showed systolic and diastolic murmurs. The systolic murmur of mitral disease was studied in detail in the 82 cases (1) The *intensity* of the murmur was labelled as "loud" in 33 cases and "soft" in 43 (2) In *character* the murmur was described as "blowing" in 47 cases and "harsh" in 27 (3) The murmur was localized to the mitral area in 48 cases, generalized or precordial in 31 and confined to the third left inter-space in 3 (4) It was *conducted* to the axilla in 55 cases and not conducted in 27 (5) An accompanying systolic *thrill* was described in 3 cases only

Features to note about the systolic murmur are (1) the systolic murmur of mitral disease though usually described as "soft" and "blowing" is quite frequently "harsh" and "loud" (2) Conduction to the axilla is not a constant feature of this murmur (3) A systolic thrill is seldom associated with this murmur

Diastolic Murmurs—A diastolic murmur was noted in 52 cases of mitral disease. It was due to mitral stenosis in every case. It was studied in detail (1) *Timing*. It was "presystolic" in 38 cases, "diastolic" in 13 and "early diastolic" in 1 (2) The *intensity* was noted as "loud" in 15 cases and "soft" in 7 (3) In *character* it was described as "rumbling" in 17 cases, "harsh" in 10 and "blowing" in 14 (4) *Localization*. It was confined to the mitral area in 40 cases, heard in the mitral and tricuspid areas in 2 and in the mitral area and base of the heart in 2 (5) *Conduction*. In 37 cases, it was not conducted in any direction, in 2 cases, it was conducted to the axilla and in 2 towards the xiphisternum (6) An accompanying *thrill* was described in 29 cases

General Appearance—Pallor of skin and mucosae was observed in 30 per cent of cases, cyanosis in 20 per cent, clubbing of the nails in 20 per cent and icterus in 3 per cent. Taking the whole series into consideration, the incidence of cyanosis and clubbing was high in the mitral group

Neck Veins—Engorgement of neck-veins was noted in 84 per cent of cases and pulsation in 51 per cent

Liver, Spleen and Ascitis—The liver was "slightly tender" in 37 per cent of cases, "markedly" tender in 46 per cent and "not tender" in 17 per cent. Tenderness of the liver was therefore noted in 83 per cent of cases of mitral disease

In 8 per cent of cases there was "slight enlargement" of the liver in 49 per cent "moderate enlargement", in 31 per cent "great enlargement" of the liver and in 12 per cent "no enlargement" Enlargement of the liver was, therefore noted in 88 per cent of cases

Splenic enlargement was noted in 20 per cent of cases *Ascitis* was noted in 40 per cent, it was "small" in 15 per cent and "massive" in 25 per cent

Oedema —In 12 per cent of cases, there was no oedema at all, in 50 per cent oedema was confined to the lower extremities in 10 per cent it was noted in the lower extremities and face, in 5 per cent, it was noted in the lower and upper extremities, in 20 per cent, it was noted in the face, upper and lower extremities, it was confined to the face in 3 per cent

The Pulse —The pulse rate on admission ranged from 64 to 160, with an average of 103 per minute In only 4 cases, was it below 75 per minute In the majority of cases, where the volume of the pulse was reported upon it was described as "weak" or "poor volume pulse"

Auricular Fibrillation was noted in 19 cases (19 per cent).

Extrasystoles were observed in 16 per cent of cases

Respiration Rate —This ranged from 20 to 40 per minute on admission, with an average of 25 per minute

Blood Pressure —The systolic pressure ranged from 80 to 125 mm, with an average of only 99 mm Hg The mitral group showed the lowest average for systolic pressure The diastolic pressure ranged from 40 to 110 mm with an average of 72 mm Hg The pulse pressure ranged from 10 to 57 mm with an average of only 26 mm Hg The low average value of the pulse pressure should be noted

Blood Reaction for Syphilis —This was positive in 3 per cent of cases only The incidence of syphilis in the aortic group was 16 times that in the mitral group

THE "AORTIC GROUP" —There were 44 cases in this group (7.3 per cent of the series)

Duration of Symptoms before Admission —The average duration of symptoms of failure before admission was 9 months, the range being 4 days to 5 years The average duration of symptoms in aortic cases was three times that of mitral cases

Presenting Symptoms —Dyspnoea was a presenting symptom in 88 per cent of cases, "cardiac asthma" in 42 per cent, cough in 28 per cent, Oedema in 23 per cent, chest pain in 10 per cent and abdominal pain in 5 per cent Features to note are (1) the high incidence of "cardiac asthma" (2) the low incidence of oedema and (3) the absence of palpitation and vertigo as symptoms

Heart Size —In 14 per cent of cases, the heart-size was reported as "normal", in 19 per cent as "slightly" enlarged, in 23 per cent as "moderately" enlarged and in 44 per cent as greatly enlarged. Enlargement was therefore noted in 86 per cent of cases, "massive heart" were observed in almost a half of the cases. Enlargement of the heart to the right was noted in 5 per cent of cases.

Character of the Apex Beat —This was described as "heaving" in 50 per cent, "feeble" in 25 per cent and "normal" in 25 per cent.

Heart Murmurs —Murmurs were described in all cases of aortic disease. Systolic murmurs were noted in 27 cases (62 per cent) and diastolic murmurs in 34 cases (77 per cent). In many as 10 cases (23 per cent) of aortic regurgitation, diastolic murmurs were not heard. The high incidence of systolic murmurs in cases of pure aortic regurgitation deserves mention, they do not necessarily mean associated aortic stenosis.

Systolic Murmur —Systolic murmurs were (1) *aortic* or basal in 12 cases (27 per cent of cases of the aortic group), "harsh" or "loud" in 8 cases and "soft and blowing" in 4. A systolic thrill was felt in 4 cases. (2) *mitral* or apical in 8 cases (18 per cent of aortic cases). The murmur was described as "soft and blowing" in all cases. No thrill was described. (3) *Precordial* or generalized in 6 cases (14 per cent of aortic cases). In 2, a systolic thrill was noted. (4) *Localized* to the third left interspace in one case.

Diastolic Murmur —Diastolic murmurs were noted in 77 per cent of cases. (1) *Site of maximum intensity*. In 11 cases, the murmur was heard best in the aortic area, (32 per cent of aortic diastolic murmurs). In 15 cases it was heard best in the 3rd and 4th left interspace (44 per cent of murmurs). In 6 cases, it was heard best in the aortic area and in the third left space. In 2 cases, it was maximum in the mitral area. The aortic diastolic murmur showed a predilection for the third or fourth left interspace in almost one-half of the cases. (2) *Character* —The murmur was described as "blowing" in 31 cases (91 per cent) and "rumbling" or "grating" in 3 (9 per cent). (3) *Intensity*. This was described as "soft" in 23 cases (68 per cent) and "loud" in 11 cases (32 per cent). (4) *Direction of selective propagation*. The murmur in 18 cases (53 per cent) was conducted downwards along the sternum. In 14 it was conducted to the apex of the heart (41 per cent) and in 2 cases, it was not conducted at all (6 per cent). An associated *thrill* was described in one case only (3 per cent).

General Appearance —Pallor of skin and mucosae was reported in 36 per cent of cases only. This is surprising in view of the classical description of aortic regurgitation with pallor. Cyanosis was noted in 14 per cent of cases, clubbing of nails in 5 per cent and icterus in 5 per cent.

Neck Veins —Engorged veins were described in 64 per cent of cases and pulsating veins in 25 per cent. The marked discrepancy between the two figures should be noted.

Liver, Spleen and Ascitis —The liver was "slightly" tender in 32 per cent, "markedly" tender in 36 per cent and "not tender" in 27 per cent. In 18 per cent of cases, there was "slight enlargement" of the liver, in 36 per cent "moderate enlargement", in 32 per cent "great enlargement" and in 14 per cent "no enlargement".
Splenic enlargement was noted in 19 per cent of cases and *Ascitis* in 37 per cent.

The Pulse —The pulse rate on admission ranged from 84 to 165 per minute, with an average of 123. The average pulse rate was much higher in the aortic group than in any other group of failure cases. Tachycardia is a characteristic feature of aortic regurgitation.

A "collapsing" or "water-hammer" pulse was described in 100 per cent of the cases. Extrasystoles were reported in 9 per cent of cases only.

Respiration Rate —This ranged from 22 to 40 per minute, with an average of 27.

Blood Pressure —Many interesting phenomena were observed in this group in connection with the arterial blood pressure.

Blood Pressure in the Upper Extremity —The systolic pressure ranged from 90 to 170, with an average of 134 mm Hg. The high average for systolic pressure, in spite of cardiac failure, should be noted; there is a definite tendency towards systolic hypertension in cases of aortic regurgitation. The diastolic pressure ranged from 0 to 70 mm with an average of 35 mm. In about 30 per cent of cases, the diastolic value was reported as 0 mm. The average value for diastolic pressure was much lower in the aortic group than in any other group of failure cases. The pulse pressure ranged from 30 to 170 mm with an average of 102 mm. Features to note are (1) the extremely wide range of pulse pressure and (2) the extraordinarily high average value. The average pulse pressure instead of being about 50 per cent of the diastolic pressure was actually three times as great. In 50 per cent of cases, the pulse pressure value exceeded 100 mm Hg, in only 5 per cent of cases was the pulse pressure less than 50 mm Hg.

(2) **Blood Pressure in the Lower Extremity** —Systolic pressure in the leg ranged from 160 to 280 mm with an average of 205 mm Hg. The diastolic pressure ranged from 0 to 65 mm with an average of only 24 mm Hg. The pulse pressure ranged from 95 to 280 mm, with an average of 181 mm Hg. Features to note are (1) the extraordinarily high systolic and differential pressures and (2) the low diastolic pressures.

(3) **Blood pressure readings in the Upper and Lower extremities compared** —The difference between the systolic pressure in the upper and lower extremities varied from 20 to 115 mm in the 44 cases, with an average value of 61 mm. The diastolic difference varied from 0

to 30 mm with an average of 10 mm Hg. The pulse pressure difference varied from 10 to 115 mm with an average of 56 mm Hg. The main difference between the pressure readings of the two extremities lies in the systolic pressure, this causes a corresponding discrepancy in pulse pressure readings. Diastolic pressure differences are negligible. In all aortic cases, blood pressure readings were higher in the lower extremity with but one exception, in this case, the diastolic pressure was reported as 35 mm Hg in the upper and as 0 mm Hg in the lower extremity.

(4) Blood pressure readings in the right and left upper extremities compared. Blood pressure readings in both the upper extremities were reported on in only 9 cases of aortic regurgitation. In all these cases, the systolic pressure was higher in the right arm, the difference in the two arms varying from 20 to 50 mm with an average difference of 35 mm Hg. The diastolic pressure, on the other hand, was higher in the left arm in all cases, the difference in the two arms varying from 2 to 50 mm with an average value of 26 mm Hg. The pulse pressure was considerably higher in the right arms in all the 9 cases, the difference between the two arms varying from 20 to 85 mm, with an average difference of 61 mm Hg.

Blood Reactions for Syphilis—These were reported as positive in 48 per cent of cases. 11 cases of aortic regurgitation were definitely rheumatic in origin. In many case records, no reference was made with regard to the blood reactions for syphilis.

THE HYPERTENSIVE GROUP—There were 41 cases in this group (6.8 per cent of the series). 25 cases (60 per cent) were classed as "Essential Hypertension", 6 (15 per cent) as "Nephritic hypertension" and 6 (15 per cent) as "Syphilitic Hypertension". The remaining 4 cases (10 per cent) were not classified.

Race—Of the 41 cases of Hypertensive failure, 16 were Hindoos, 11 Muslims and 14 Christians. The relative preponderance of Christians in this group was noted.

Sex—There were 23 males and 18 females giving a ratio of males to females of 1.3 to 1.0. The relative preponderance of females in this group should be noted.

Age Distribution—Patients varied in age from 25 to 80 years, in this group, the average being 43 years. In the case of males, the range was 25 to 80 years and the average 45 years. In the case of females, the range was 27 to 70 years and the average 43 years.

Duration of Symptoms before Admission—The average duration was 4.5 months, the range being 2 months to 2 years.

Presenting Symptoms—Dyspnoea was a presenting symptom in 72 per cent of cases, oedema in 45 per cent, cough in 40 per cent, vertigo in 25 per cent, hoarseness of voice in 10 per cent, chest pain

in 10 per cent and abdominal distension in 5 per cent. The high incidence of vertigo and hoarseness of voice should be noted.

Heart Size —In 10 per cent of cases, the heart was "normal" in size, in 25 per cent it showed "slight" enlargement, in 30 per cent "moderate" enlargement and in 35 per cent "great" enlargement. In 90 per cent of hypertensive cases, there was enlargement of the heart. Massive hearts are common in hypertension.

Character of Apex Beat —This was described as "normal" in 20 per cent, as "heaving" in 75 per cent and "weak" or "feeble" in 5 per cent.

Heart Sounds —The *first sound* was described as "normal" in 30 per cent of cases, as "muffled" or "distant" or "weak" in 25 per cent and as "accentuated" or "thudding" in 45 per cent. The *second sound* was described as "normal" in 15 per cent, as "weak" in 10 per cent and as "accentuated" in 75 per cent. The heart sounds tend to show increased intensity in cases of hypertensive failure.

Heart Murmurs —Murmurs were reported in 44 per cent of cases. In all cases, they were "systolic" in time. The systolic murmur of hypertension displayed the following characteristics, (1) Site of maximum intensity. This was the mitral area in 10 cases, the aortic area in 6 cases and the whole of the precordium in 2 cases. (2) Intensity. This was described as "harsh" or "loud" in 3 cases and as "soft" in 15 cases. (3) Character. The murmur was "blowing" in character in all cases. (4) Conduction. Conduction to the axilla was reported in 5 cases. (5) Thrill. An accompanying systolic thrill was described twice, in both cases it was maximal in the aortic area. Diastolic murmurs were not observed in any of the cases.

General Appearance —Pallor of skin and mucosae was noted in 20 per cent of cases, and cyanosis in 40 per cent, the high incidence of cyanosis should be noted. Clubbing and icterus were not observed in this group.

Neck Veins —Engorgement of veins was noted in 45 per cent and pulsation in only 10 per cent. Venous phenomena are not prominent in this group.

Liver, Spleen and Ascitis —The liver was tender in 70 per cent and, "not tender" in 30 per cent. The tenderness was "slight" in 40 per cent and "marked" in 30 per cent. Enlargement of the liver was noted in 70 per cent. It was "slight" in 10 per cent, "moderate" in 50 per cent and "great" in 10 per cent. Enlargement of the liver was absent in 30 per cent of cases.

The spleen was enlarged in 5 per cent of cases only. Ascitis was noted in 40 per cent, it was "small" in 10 per cent and "massive" in 30 per cent.

Oedema —In 10 per cent cases there was no oedema at all, in 35 per cent, oedema was confined to the lower extremities, in 35 per cent

cent, it was noted in the lower extremities and face, in 20 per cent, it was noted in the face, upper and lower extremities. Oedema of the lower extremities was, therefore, noted in 90 per cent of cases, of the upper extremities in 20 per cent and of the face in 55 per cent. The high incidence of oedema of the face in this group should be noted. In only 5 per cent of cases did oedema of the face precede oedema elsewhere.

The Pulse —The rate on admission varied from 62 to 128 with an average of 88 per minute. The average was low in spite of cardiac failure. There appear to be two groups of hypertensive failure cases: (1) The *bradycardiac group* with low pulse rates. There were 17 cases in this group with pulse rates ranging from 62 to 90 and an average pulse rate of 81 per minute. (2) The *tachycardiac group*, with high pulse rates. There were 24 cases in this group with pulse rates ranging from 100 to 128 per minute, the average for this group being 116 per minute. Extrasystoles were observed in as many as 35 per cent of the cases.

Respiration Rates —This varied from 20 to 36 per minute on admission, with an average of 26 per minute.

Blood Pressure —The systolic blood pressure ranged from 150 to 230 mm Hg, with an average of 183 mm.

Cases could be classified into two groups on the basis of the systolic pressure: (1) Cases with systolic pressure values between 150 and 180 mm Hg. There were 25 cases in this class (60 per cent), (2) cases with systolic values over 200 mm. There were 15 cases in this class (38 per cent). The average value for systolic pressure was 166 mm in class (1) and 210 mm in class (2). The diastolic pressure ranged from 90 to 130 mm Hg, with an average of 112 mm Hg. The pulse pressure ranged from 40 to 100 mm, with an average of 71 mm Hg. In the hypertensive group, the average systolic, diastolic and pulse pressure values were all high.

Blood Reactions for Syphilis —These were "positive" in 4 per cent of cases only.

Blood Count —The red cell count varied from 3.2 to 4.8 millions per c.m.m., with an average of 4 millions.

The haemoglobin percentage varied from 65 per cent to 92 per cent, with an average of 79 per cent. The colour index varied from 0.9 to 1.0 with an average of 0.98. The white cell count varied from 6,000 to 11,300 with an average of 8,400 cells per c.m.m.

Urinary Findings —The specific gravity of urine varied from 1.001 to 1.018 with an average of only 1.009.

Albuminuria was reported in as many as 80 per cent of the cases: in 30 per cent it was "slight", in 30 per cent "moderate" and in 20 per cent "severe". Granular casts were reported in 55 per cent of

cases, in 40 per cent, in small numbers and in 15 per cent in large numbers Pus cells noted in 35 per cent of cases, in small numbers in 20 per cent and in abundance in 15 per cent Features to note about the urine are (1) the low specific gravity (2) the great tendency to albuminuria and (3) the high incidence of granular casts

MYOCARDIAL DEGENERATION OR CORONARY SCLEROSIS

Though labelled "myocardial degeneration" the great majority if not all of the cases in this group appear to be examples of coronary sclerosis There were 38 cases in this group (6.3 per cent of the whole series) In 15 cases (39 per cent), a definite history of coronary thrombosis was obtained In 16 cases (42 per cent) the condition was described as "acute" and in the remaining 22 cases (58 per cent) as "chronic"

Race —There were 26 Hindoos, 7 Muslims and 5 Christians

Sex —There were 27 males and 11 females, giving a ratio of males to females 2.6 to 1.0

Age Distribution —The age range was 22 to 78 years, and the average age 48 years It is important to realize that coronary disease is essentially a disease of middle age

Duration of Symptoms —The average duration was 5 months and the range 4 days to 2 years

Presenting Symptoms —Dyspnoea was a presenting symptom in 90 per cent of cases, oedema in 46 per cent, chest pain in 42 per cent abdominal pain in 22 per cent, distension of the abdomen in 17 per cent, cough, ascitis, palpitation and fever each in 11 per cent and insomnia in 6 per cent Features to note are the high incidence rates of dyspnoea and chest pain in this group In no other group of failure cases was there such a high incidence of chest pain

Heart Size —This was classed as "normal" in 36 per cent, as "slightly" enlarged in 48 per cent and as "moderately" enlarged in 16 per cent "Great" enlargement of the heart was not observed in this group In this group therefore as many as 84 per cent of cases showed normal or only "slightly" enlarged hearts

Heart Sounds —The *first sound* was described as "normal" in 45 per cent of cases, as "muffled" or "weak" in 50 per cent and as "accentuated" in 5 per cent The *second sound* was "normal" in 22 per cent, "weak" in 56 per cent and "accentuated" in 22 per cent There is a high incidence of "muffled" sounds in this group

Heart Murmurs —Murmurs were described in only 11 per cent of cases In all cases, they were systolic in time

(1) The *site* was described as "precordial" in all cases (2) In intensity and character the murmur was described as "soft and blow-

ing" in all cases (3) Selective propagation of the murmur was not observed in any case

General Appearance —This was described as "pale" in 34 per cent and as "cyanotic" in only 6 per cent Icterus was not observed in any of the cases Clubbing occurred in 11 per cent of cases

Neck Veins —Engorgement was noted in 46 per cent and pulsation in 34 per cent

Liver, Spleen and Ascitis —The liver was tender in 51 per cent of cases only It was "slightly" tender in 34 per cent and "markedly" tender in 17 per cent

Enlargement of the liver was noted in 56 per cent of cases, it was "slight" in 12 per cent and "moderate" in 44 per cent Severe degrees of hepatomegaly were not observed in this group The spleen was found enlarged in 11 per cent of cases only

Ascitis was noted in 11 per cent

Oedema —In 44 per cent of cases, there was no oedema at all In 34 per cent, oedema was confined to the lower extremities, in 16 per cent, it was noted in the lower extremities and face and in 6 per cent it was noted in the face, upper and lower extremities Practically one-half of the cases in this group were free of oedema

The Pulse —The rate on admission varied from 80 to 160 per minute with an average of 103 per minute

Respiration Rate —This varied from 24 to 38 per minute with an average of 28 per minute

Blood Pressure —The systolic pressure ranged from 90 to 140 mm, with an average of 116 mm Hg The diastolic pressure ranged from 50 to 90 mm with an average of 78 mm Hg The pulse pressure ranged from 22 to 60 mm with an average of 38 mm Hg

Blood Reaction for Syphilis —This was "positive" in 6 per cent of cases only

Pulmonary Congestion —This was noted in only 47 per cent of cases in this group

VITAMIN B DEFICIENCY OR BERI-BERI GROUP

There were only 10 cases allotted to this group Such an apparent low incidence is perhaps due to the difficulty experienced in the diagnosis of Vitamin B Deficiency Minor degrees of Vitamin B deficiency are liable to be missed unless full use is made of the laboratory

Sex —There were 6 males and 4 females, giving a ratio of males to females of 1.5 : 1.0

Age —The average age was 37 years and the range 16 to 60 years

Duration of Symptoms —The average duration was 2 months and the range 15 days to 6 months. The low average suggests a rapidly progressive development of failure in this group of cases.

Presenting Symptoms —Oedema was a presenting symptom in 100 per cent of cases, dyspnoea in 80 per cent, diarrhoea in 60 per cent, anorexia in 50 per cent, debility in 40 per cent and indigestion in 20 per cent. Features to note in this group are (1) the occurrence of oedema in all cases and (2) the high incidence of gastro-intestinal symptoms, like diarrhoea and anorexia.

Heart-Size —In 60 per cent of the cases, the heart-size was described as "normal" and in 40 per cent as "slightly" enlarged. Note the absence of "large hearts" in this group. Right-sided enlargement was observed in as many as 40 per cent of the cases.

Heart Sounds —The first sound was "normal" in 10 per cent and "muffled" or "weak" in 90 per cent of cases. The second sound was "normal" in 20 per cent and "muffled" or "weak" in 80 per cent. The characteristic feature observed in this group on auscultation was "muffling" of the sounds.

Heart Murmurs —A systolic murmur, soft and blowing in character, heard all over the precordium and not conducted in any direction, was reported in 1 case only (10 per cent).

General Appearance —Pallor of the skin and mucosae was described in as many as 60 per cent of the cases. Cyanosis, clubbing and icterus were not reported in any of the cases. Note the high incidence of pallor and the absence of cyanosis and clubbing in this group.

Liver, Spleen and Ascitis —The liver was reported as tender in 30 per cent of cases only, it was enlarged in only 40 per cent of cases. The spleen was enlarged in 10 per cent while ascitis was noted in as many as 60 per cent of the cases.

Oedema —In 40 per cent of cases, Oedema was confined to the lower extremities, while in 60 per cent it was observed in the lower extremities and face. In 20 per cent of cases oedema of the face preceded oedema of the legs. The high incidence of facial oedema (60 per cent) should be noted.

The Pulse —The rate on admission varied from 80 to 130 per minute, the average being 100 per minute.

Respiration Rate —The rate varied from 22 to 32 with an average of 27 per minute.

Blood Pressure —The systolic pressure ranged from 95 to 115 mm with an average of 108 mm Hg, the diastolic pressure ranged

from 0 to 78 mm with an average of 68 mm Hg The pulse pressure ranged from 35 to 40 mm with an average of 42 mm Hg

THE UNCLASSIFIED OR OBSCURE GROUP

In this group of 74 cases (12.3 per cent of the whole series) the aetiological factor or factors concerned in the genesis of cardiac failure remained obscure Study of the case records showed that lack of diagnosis in the majority of cases was explainable on one of the following grounds (1) Lack of proper history-taking This was in many cases unavoidable on account of the patient being admitted unconscious or in a moribund state, too ill to give a history (2) Inability to examine or investigate the case on account of some associated disease or deformity e.g. acute pulmonary oedema, emphysema, chest, spinal deformity etc (3) Lack of proper examination of the patient or lack of necessary laboratory investigations It is suggested that a fair number of cases included in the obscure group, in the present series, would probably have been classified as "Beri-beri Heart" or "Thyrotoxic heart" if the necessary laboratory investigations had been carried out (4) Inadequate stay in hospital on the part of the patient, allowing little or no time for proper investigation

In some cases, patients "walked out" of Hospital against medical advice, in other cases, they expired within a few hours of admission before any diagnosis could be arrived at

After excluding the above groups of cases there remained only about 26 cases which could be regarded as "truly obscure" In these cases, in spite of full history taking, thorough clinical examination and adequate laboratory investigation, the diagnosis still remained obscure

In this group of 26 cases (4.3 per cent of the series) lack of diagnosis can be considered unavoidable, in the present state of our knowledge The incidence of "obscure cases" is definitely higher in tropical countries than in temperate climates, a fact borne out by the majority of clinicians and which is probably accounted for by two factors (1) The multiplicity of aetiological factors in the tropics and (2) lack of efficient laboratory aid in tropical countries

Further study of this group may serve to unravel some of the obscure problems connected with the aetiology of heart failure in the tropics

orders. But the dosage was inadequate and the results rarely satisfactory, its action was not understood and there were no definite indications.

Only at the beginning of this century, the work of Cushny, Mackenzie and Lewis demonstrated the slowing of the ventricular rate in cases with auricular fibrillation and the chief indication for the use of digitalis was considered to be cardiac failure with auricular fibrillation and tachycardia. Little emphasis was laid on its action on the ventricular muscle and on the results produced in cases of failure with regular rhythm.

Unfortunately its use continued and still continues at present in some quarters, as a medical ritual, in patients with a supposed "weak pulse", "weak heart" acute infections, such as pneumonia, or septicaemia, after or before operations, tachycardias of various origins, neuroses or thyroid disease in the vague hope "to tone up the heart", or to support the circulation, and as an injection to dying patients as a sort of a final magic wand!

INDICATIONS AND CONTRAINDICATIONS

The pharmacological experimental work and the clinical experience of the last thirty years have shown that the chief action of the drug is on the ventricular muscle and that it produces surprisingly good therapeutic results in all cases of congestive cardiac failure with or without arrhythmia or tachycardia.

The chief *indication* for the use of digitalis is the presence of cardiac failure, either right and left ventricular, or predominantly left ventricular, irrespective of its cause, with or without tachycardia and with regular or irregular rhythm. On the earliest manifestation of the muscle failure digitalis should be exhibited. The presence of cardiac breathlessness, oedema, venous engorgement, hepatic tenderness and enlargement, cyanosis, basal rales, hydrothorax, nocturnal cough or dyspnea, Cheyne-Stokes breathing, or acute pulmonary oedema, is a definite indication for the administration of digitalis in adequate doses.

Hypertension associated with paroxysmal breathlessness, without peripheral oedema or congestion, and paroxysmal arrhythmias without cardiac failure are also greatly benefited by digitalis.

In the presence of peripheral oedema of obscure origin digitalis may be used as a therapeutic test. It is also useful in the stage preceding the use of quinidine in cases of paroxysmal auricular fibrillation and flutter.

Some clinicians have advocated the use of digitalis in small doses for long periods in cases of myocardial weakness in the aged and in persons with enlarged hearts from any cause at any age.

It is now well established that in cases of heart failure where the auricles are fibrillating and the ventricular rate is rapid, digitalis will reduce the ventricular rate and will produce a spectacular clinical im-

provement But the slowing of the heart rate does not occur when the rhythm is regular In fact the presence of tachycardia in itself is not an indication for the use of digitalis Tachycardia very often is a result of abnormal circulation, the rate being adjusted to the body's requirements Here no direct attempt is necessary to reduce the rate The rapid heart rate of pneumonia, tuberculosis, malaria, neurosis, thyrotoxicosis and collapse is not affected by digitalis, and indeed, from other physiological considerations also, digitalis is not indicated in these states in the absence of congestive cardiac failure In paroxysmal tachycardias quinidine is more effective than digitalis

Digitalis should not be given to a patient having *ephedrine* or *calcium* Simultaneous use of *digitalis* and *ephedrine* is dangerous There is experimental evidence to show that animals were killed with about half the average lethal dose of *ephedrine* in the presence of about half the medial lethal dose of *digitalis* Similarly, in the presence of full digitalization, exhibition of *calcium* or *barium* are dangerous Very small doses of intravenous *calcium* have proved fatal in persons on full doses of *digitalis*

Morphia and *atropine* may be used safely with *digitalis* when required They in no way affect the *digitalis* effect *Quinine* and *strychnine* are said to enhance the action of *digitalis*, especially in cases of paroxysms of extrasystoles

In *Angina pectoris*, without heart failure, the use of *digitalis* is likely to increase the frequency and severity of the attacks and it is best avoided But when signs of congestive failure appear *digitalis* may be used without fear The heart failure in these cases is more often of the left ventricular type It is a remarkable fact not yet explained, that cases of *angina pectoris* lose their pain when congestive cardiac failure supervenes

At the onset of *Coronary thrombosis*, when there is marked shock or circulatory failure, *digitalis* is useless Its use at this stage is even fraught with danger, as it is likely to increase the muscular irritability and produce a fatal ventricular fibrillation Later, when signs of congestion appear it may be used, but with caution The real danger of excessive dosage in these patients should always be kept in mind and under no condition should the optimum dose be exceeded

In *thyrotoxicosis* the presence of tachycardia or even auricular fibrillation is no indication for the use of *digitalis* The tachycardia is the result of enhanced metabolism and auricular fibrillation a result of toxic action of the abnormal thyroid secretion on the myocardium, and are not expected to be affected by *digitalis* *Digitalis* should only be used if there is congestive failure or if it is thought to be imminent Its use before or after operations on the thyroid is not justified by the results, on the contrary its routine pre or postoperative use has proved to be definitely harmful

In cases of *shock*, *collapse* or *peripheral failure* from any cause, *digitalis* is not indicated Circulatory failure or tachycardia in acute infections such as pneumonia malaria, septicaemia, meningitis is

not improved by digitalis in any way, in fact there is enough clinical evidence that the routine use of digitalis in acute infections is associated with a higher mortality rate. There is no justification for its use in *acute infections* except the presence of congestive failure or auricular fibrillation, there is less justification for its use in typhoid fever, diphtheria, and acute rheumatic fever where there is already increased vagal tone, a relatively slow pulse, and at times a fair degree of heart block or focal myocarditis. Similarly in *surgical conditions* associated with collapse, or collapse before or after labour, digitalis is valueless. Injections of small subtherapeutic amounts of digitalis in these cases is a remnant of old practice producing no effect in the patient, but a feeling in the practitioner that something is done. But this need not take the place of more effective and urgently needed measures.

In cases of recent *embolism* either pulmonary or systemic the use of digitalis is withheld for fear of the more powerful muscular contractions and a release of more thrombi. The risk is not very great, and if other signs warrant digitalis may be given without hesitation.

The presence of *hypertension*, *aortic regurgitation* or *aneurysm* is not a contraindication to the use of digitalis. In the presence of signs of failure, paroxysmal dyspnoea or congestion the blood pressure leading to the valvular leak or the aortic widening may be safely ignored.

In *complete heart block* digitalis cannot affect the automatism of the ventricular rate and so the patients with a ventricular rate of 25-30 beats per minute may be digitalized without any danger. As the ventricular rate is not affected by the therapeutic action of digitalis, any rise in this rate should be attributed to the toxic action of the drug on the myocardium and the optimum dose regulated accordingly.

In *partial heart block*, however, the heart rate may be lowered by digitalis and a state of complete block established. Therapeutically a-v block is produced in cases of auricular fibrillation and auricular flutter to reduce the heart rate. It is a lesser evil than ventricular failure. In the presence of myocardial failure, the conduction defect may be ignored and digitalis exhibited solely on the state of failure and the response to digitalization. But it should be admitted that sudden changes in rhythm produced by digitalis are apt to induce Adams-Stokes attacks, which occur at the time of transitions between states of partial and complete block. This possibility should be kept in mind and if the seizures become frequent, the drug may have to be omitted.

Bundle-branch block of any extent is not considered a contraindication. Though the electrocardiographic evidences of block are increased under digitalis, the clinical improvement in failure is considerable and the former may be ignored.

The presence of *extrasystoles* requires a special consideration. If these are present before digitalis is started, they very often disappear under digitalis therapy. On the other hand the appearance of extrasystoles is one of the best known digitalis effects. The amount necessary to produce extrasystoles varies within wide limits in different patients and even in the same individual. Their early appearance usually indicates the toxic action of digitalis on a diseased myocardium and to that extent suggests a poor prognosis. Their persistence raises the possibility of toxic tachycardia or fibrillation, and digitalis should be stopped for a few days. Often they do not reappear on the resumption of the drug. In most cases, however, the presence of occasional extrasystoles under digitalis may be ignored, as they tend to disappear on full digitalization.

The attack of *paroxysmal tachycardia* is rarely stopped by digitalis. Again, digitalis is known to produce a paroxysm of ectopic tachycardia. Hence it is best avoided in these cases and failing other measures, if given in the presence of failure, it should be only under carefully controlled conditions.

Auricular fibrillation of toxic origin, from infection, thyroid dysfunction or digitalis overdosage, is not affected by digitalis, it may be made even worse. In non-toxic auricular fibrillation, without heart failure, digitalis may be used, to reduce the ventricular rate, though it is not likely to abolish the arrhythmia. In non-toxic auricular fibrillation with heart failure, digitalis should be used till the failure is controlled. In toxic cases with heart failure digitalis is not likely to do much good.

In *auricular flutter* digitalis is used to increase the block and to convert the flutter into a fibrillation. Auricular flutter and fibrillation are better abolished by quinidine which acts better if used after a course of digitalis.

The use of digitalis is not contraindicated in the presence of *pulsus alternans*. But as alternation indicates grave damage to the myocardium, careless use of digitalis in such cases is more likely to produce serious toxic symptoms. Digitalis itself is known to produce *pulsus alternans* as a toxic effect.

Idiosyncrasy to digitalis is rare. Some persons are intolerant to its use and will suffer from persistent vomiting or arrhythmia. Some may not like the smell or taste. In such persons it is necessary to change the preparation, the mode of administration or even replace it by strophanthin.

THE MODE OF ACTION

The *mode of action* of digitalis is recently studied. Digitalis, administered by any route, is fixed in the heart muscle and cannot be washed out of it. At first it is inactive. Gradually it is changed by the muscle cell into a body which has a digitalis effect and which now is no longer fixed in the muscle and so slowly disappears. This explains the *interval* required to obtain and maintain a digitalis

effect as well as the digitalis poisoning. The fixation of digitalis is in proportion to the concentration of the drug in the blood and the mass of the heart muscle, and explains the variable effects of digitalis in different patients. The action of digitalis is on the diseased myocardium. It is not a circulatory stimulant. It stimulates the vagus, producing the slowing of the heart rate, it acts directly on the conducting system producing heart block, it acts directly on the heart muscle enabling it to contract more strongly and relax more easily, it improves the nutrition of the heart by increasing the coronary blood flow. In therapeutic doses it does not raise the blood pressure in man.

PREPARATIONS

The B. P. preparations of digitalis are biologically assayed and standardised. Any physician who makes himself thoroughly familiar with their proper use need not bother about the daily increasing number of proprietary preparations about whose composition and action one can never be sure, and which are always more expensive and at times unreliable. The preparations described to be non-toxic or reputed not to cause nausea, cannot be active. Whatever preparation is used it behoves the physician to use continuously the same form of digitalis in order to become thoroughly familiar with its dosage and its way of action. In cardiac therapeutics there are two variables, the reaction of the patient's heart and the potency of the digitalis preparation. It is necessary that there is certainty at least about the potency of the drug. This should not be based on the name or the word of the manufacturer but on trial and error basis of personal experience.

Recently preparations of *Digitalis lanata*, either a mixture of several glycosides such as *digilanid* or purified special preparations such as *digoxin*, have appeared on the market. They are said to be less toxic, less cumulative, being washed out of the heart muscle more rapidly than the preparations of digitalis purpurea. Clinically these preparations appear to be as effective and toxic as those from digitalis purpurea and the highly purified crystalline preparations like digoxin, require special watchfulness in regulating the dosage.

Methods of administration The oral is the method of choice because of its safety and convenience. The preparation of choice is tincture or the powdered leaf. When the potency of the preparation used is known by its action in other cardiac patients, its failure in a given case may be attributed to a lack of absorption or an inability of the heart muscle to respond. Intestinal oedema or stasis may affect the absorption and a brisk saline purge or jalap powder may help. In other cases the mode of administration may be changed. Some patients cannot take digitalis by mouth because of its smell or taste, or the gastric irritation, in the presence of portal congestion producing vomiting. Here it may be given *rectally*. The lower bowels are cleared by an enema, and the whole daily dose of

60 to 120 minims of the tincture mixed with about two ounces of 5 per cent glucose saline is left in the rectum through a rubber catheter. This may be repeated for a few days till it is possible to resume the oral route. *Intramuscular* digitalis is very rarely necessary in patients who cannot take it by mouth because of the portal congestion and vomiting or who are unable to swallow. Digitalis given intramuscularly is highly irritating. The dosage is much the same as when it is given by the mouth. Small amount of digitalis injected in patients suffering from acute infections, or before or after operations is quite useless. *Digitan*, *digifolin* or *digalen* are suitable preparations for intramuscular use if given in sufficient doses.

Intravenous digitalis is necessary only as an emergency measure in acute pulmonary oedema, or paroxysmal nocturnal dyspnoea. For this *digoxin* is a suitable preparation. It is supplied in ampoules containing 0.5 mgm dissolved in 1 c.c. of 70 per cent alcohol. Before use it is diluted ten times with sterile normal saline or water. The injection may be repeated after eight hours. When the amount of digitalis previously taken by the patient is not known intravenous digitalis should be avoided, and in no circumstances should the dose of one mgm in twenty-four hours be exceeded.

There is no effective substitute for digitalis. Preparations of *scilla* have been used in persons who cannot take digitalis, and *scillaren* injections are used to produce diuresis but with rarely satisfactory results. *Strophanthin*, allied to digitalis in action, is more active and rapid, and it is indicated where a rapid digitalis effect is desired. In acute infections, before or after operations, or labour, if through the failure of the myocardium, digitalis-action is thought necessary. *Strophanthin* is a more suitable drug, because of its strength and rapidity of action. It is said to give satisfactory results in cases of aortic insufficiency, hypertension or coronary disease. In persons who cannot tolerate digitalis, *strophanthin* may be tried. The tincture *strophanthin* given by mouth is usually inert. *Strophanthin* to be effective has to be given by injections. For this purpose amorphous *g* *strophanthin* or crystalline *g* *strophanthin* or *ouabain* are available. The dose is very small, from $\frac{1}{240}$ to $\frac{1}{10}$ gr, or (0.25 to 1 mgm), and is given intravenously well diluted in normal saline. 0.25 mgm of *strophanthin* is equivalent in therapeutic effect to about one dram of tincture digitalis. This dose may be repeated after twelve hours.

Strophanthin should not be used in persons having digitalis. At least for three days the patient should be without digitalis before *strophanthin* can be given safely. On the other hand, digitalis by mouth may be given to patients soon after *strophanthin* injection, as, by the time digitalis acts, *strophanthin* effect will have subsided. Too much *strophanthin*, or *strophanthin* injection in a patient who was on digitalis before, will produce sudden death from ventricular fibrillation. A few minutes to half an hour after the *strophanthin*

injection extrasystoles develop which may increase in number, producing an alarming tachycardia. This may subside or go on to a fatal ventricular fibrillation.

THERAPEUTIC ACTION AND DOSAGE

In digitalis medication one should remember that

- (a) of the digitalis given per day, a certain amount, say 15 to 20 minims, is eliminated per day,
- (b) an accumulation in the body of, say, four to five drams is necessary before the therapeutic action is produced. This is the therapeutic, effective or optimal dose, and it varies in different persons, and is roughly proportionate to the body weight,
- (c) this amount must be maintained continuously in the body to obtain the desired effect continuously; thus the maintenance dose, after full digitalization is roughly equivalent to the amount of the digitalis eliminated per day.
- (d) When this amount—the therapeutically effective dose—often very near the maximal, is exceeded toxic symptoms are produced.

The desired digitalization may be obtained by administering a single calculated dose, large doses or small doses.

Rapid single dose digitalization within 6 to 12 hours is rarely required and indeed it is not desirable. In most cardiac patients it is impossible to be quite sure of the amount of digitalis taken before nor can one foresee the idiosyncrasy or the intolerance for the drug. Again, the calculated therapeutic dose though correct for most cases is either too big or too small for some patients. In a very occasional cardiac case where one may consider the need for rapid digitalization, intravenous digoxin or ouabain may be used.

Large dose digitalization is useful in severe or extreme failure where it is thought advisable to digitalize the patient in a day or two. Here half the calculated amount may be given immediately, and the half of the remaining dose, six hours after, and if desired, the remaining half may be given in equal parts at six hourly intervals. Thus a man weighing 140 lbs and needing $140 \times 0.15 = 21$ cc of tincture may receive 10 cc, 6 cc, 3 cc, 2 cc at six hourly intervals. This method is quite safe if the patient is under continuous observation, where it is possible to omit the last doses if the desired effect is obtained early, or if toxic symptoms have appeared. Very large amount of digitalis even if warranted by the calculated dose should never be used. It rarely does good and not infrequently produces severe toxic manifestations.

Small dose digitalization is the safest and most commonly used method in practice, in cases which are not in extremis. 30 minims of the tincture in advanced failure, 20-25 minims in moderate failure, and 15-20 minims in slight failure, given three or four times a

day, will show the desired therapeutic effect in 2 to 4, 4 to 7, and 7 to 10 days respectively. By increasing or decreasing the dose of digitalis the period of digitalization may be regulated as desired. It takes about six hours for digitalis to get absorbed, and become fully effective, so the time interval between two doses should not be less than six hours.

The therapeutic dose of digitalis is very near the toxic dose. In fact some clinicians believe that mild toxic symptoms always precede the full therapeutic effect. At first Withering's custom was to order one dose to be taken after the sickness commenced, for at that time he thought it necessary to bring on and continue the sickness. Careful study however taught him that nausea was not at all necessary. Some advise the starting of the maintenance dose of digitalis on the third day after the digitalizing quantity has been determined, that is, three days after the first appearance of minor symptoms of intoxication. It must be emphasised that to produce a full therapeutic result the calculated dose, or the maximal tolerated dose is not always the optimal therapeutic dose. An amount well below the calculated tolerated dose often produces satisfactory therapeutic response and that dose need not be exceeded. This optimal dose varies in different individuals and according to the degree of the myocardial failure in the same individual. This dose can be found only by trial and error and noting the therapeutic response in each individual case from day to day.

This response to digitalis therapy is judged not by the alteration in the pulse rate but by the disappearance of the circulatory distress as shown by better breathing, sleep, diuresis, fall in body-weight and a fall in the venous pressure. The patient is more comfortable, complains less, and feels a great relief and a new sense of well being. The pulse may remain rapid or normal or the pulse deficit may disappear, with the slowing of the ventricular rate. Actual slowing of the heart rate is not a therapeutic effect of digitalis but a toxic one.

The average maintenance dose also varies in different individuals and it roughly follows the elimination rate, which varies with the amount of the drug in the body. No fixed quantity can be prescribed as a maintenance dose, which requires to be worked out individually. Daily average excretion of digitalis after a full digitalization is about 15 to 20 minims. So a dose of seven minims three times a day may be taken as a working hypothesis. This maintenance dose may be given indefinitely if no nausea or vomiting is produced. Or a slightly bigger dose, determined by trial, just enough to produce nausea in five to seven days may be given with instructions to omit the drug for two days at the first appearance of unpleasant symptoms. Thus, digitalis may be given for five days in a week, and omitted for two days. These shorter courses of five digitalis days with two free days are better than longer periods of ten or fourteen days. The dosage must be increased on the earliest manifestation of imminent failure.

TOXIC MANIFESTATIONS

A thorough acquaintance with the toxic manifestations of digitalis is necessary for its proper use. These follow a regular sequence and may be grouped as follows —

- (1) frontal headache and anorexia,
- (2) nausea and vomiting,
- (3) minor arrhythmias sinus, and extrasystoles,
- (4) diarrhoea,
- (5) yellow or green vision, or amblyopia, or red or blue vision, scotomata, or diplopia,
- (6) delirium, hallucinations and mental confusion,
- (7) multiple extrasystoles, coupling of beats or bigeminy slowing of pulse rate under 50 per minute, complete heart block with a rate under 35 per minute, paroxysmal tachycardia, auricular fibrillation, alternation of the heart, or ventricular fibrillation

Frontal headache and anorexia followed by nausea and vomiting easily recognised by the patient as due to the drug, are the earliest manifestations of digitalis intoxication, and indicate the reduction of the dose or the withdrawal of the drug for a few days. Nausea and vomiting in cardiac patients may occur as a result of gastric irritation due to portal congestion. In such cases the vomiting is early, and soon after the dose of digitalis, and is no indication for the withdrawal of the drug, but rather an indication for the full digitalization. The method of administration of the drug may be changed, it may be given in a more diluted form, or per rectum, or by injection. The nausea and vomiting due to digitalis poisoning are not due to the local gastric irritation but are *reflex* results after a sufficient amount of the drug is absorbed and there is a definite action on the heart muscle as shown by the electrocardiographic changes. The vomiting is central, the medulla being stimulated by the afferent impulses from the heart through the sympathetic or the vagi. The digitalis vomiting is always preceded by a period of anorexia and nausea, and *it appears after an appreciable time interval, in successive waves, with periods of relative freedom disappearing completely a few days after the drug is withdrawn.* It is not affected by a change in diet or by sedative drugs.

The appearance of minor arrhythmias such as sinus arrhythmia, extrasystoles, and a prolongation of a-v interval should be taken as warning signals. Often these disappear when the patient is fully digitalized but if they persist or get worse, the drug should be stopped for three or four days.

The appearance of diarrhoea, or visual disturbances, such as amblyopias, scotomata, colour vision, green or yellow, rarely red or blue, or diplopia suggests a severe intoxication and the drug must be immediately stopped.

Cerebral disturbances, such as mental confusion, hallucinations, and delirium are serious results of digitalis poisoning, but at times, they may be due to advanced heart failure, especially in aortic and high blood pressure cases. So are the severe cardiac manifestations such as digitalis bigeminy from ventricular extrasystoles, complete heart block, sinoauricular block, auricular fibrillation, or tachycardia, and ventricular tachycardia or fibrillation. A marked slowing of the normally beating heart is a toxic effect of digitalis and should not be taken as a beneficial therapeutic effect. The induction of tachycardia also calls for the immediate withdrawal of the drug.

There are *two special dangers* in digitalis medication after the early toxic symptoms have appeared which should be kept in mind. *First*, there is experimental evidence to show that by the repeated doses of digitalis the heart may be so sensitized to the subsequent action of the drug, that death may follow from ventricular fibrillation after taking a very small amount, and

Second, in subjects with digitalis poisoning, the early vomiting may disappear as a result of the depression of the vomiting centre and the further intoxication of the myocardium may proceed with fatal results.

Finally, "when using digitalis daily observation is absolutely essential in every case to decide how much should be given and how long the treatment should be continued. Digitalis treatment is one of the most important and serious duties of the general physician, it demands a great deal of skill, power of observation, keen interest, and experience. A long life is too short to learn enough about this wonderful drug"—Wenckebach.

Case Reports

A CASE OF ELECTRIC SHOCK

By M D MOTASHAW, M.B.B.S.

A christian male aged 24, was admitted to the K E M Hospital on 4-12-41, under the case of my chief, Dr N D Patel. The history was that he was an electrical wireman by profession and whilst at his work in a factory on the morning of the 3rd December 1941, he accidentally happened to touch a live connection with the index finger of his right hand. He was working at a height of about 12 ft and no sooner he touched the connection he was thrown off the ladder on which he was standing and fell to the ground below. According to his own statement he remained unconscious for about half an hour and when he regained consciousness, he was in a dazed condition and could not think clearly, and a strange feeling of stiffness pervaded the entire musculature of his body. The same afternoon he developed a temperature with a slight cough. Next morning the temperature increased, so he came to the hospital and was admitted for observation. The patient had no fever before he had received the electric shock.

On the tip of the index finger of his right hand was a circular area $\frac{1}{4}$ " in diameter. The epidermis over this area was white and gave the appearance of a slough. There was no inflammatory reaction round about this area. There were a few abrasions on the ulnar border of his left forearm. No injury could be clinically detected in the region of the left hip joint or the perineum. Nothing abnormal was found by a routine examination of his alimentary, respiratory, cardiovascular, and nervous systems. Liver, spleen, or glands were not palpable. His BP was 108 mm Hg systolic and 78 mm Hg diastolic.

The afternoon after his admission, 5-12-41, his temperature rose to 102° F, pulse 120 and respiration 28 per minute. At this time a blood smear was taken which showed white blood cells 8950 per cmm. A differential count of 200 cells showed polymorphs 64 per cent, eosinophils 2 per cent, lymphocytes 30 per cent, large mononuclears 4 per cent. No Malarial parasites were seen. Urine showed no abnormality. By 10 p.m. the same day his temperature had risen to 103° F with pulse 124 and respiration 28 per minute. The next morning his temperature dropped to 98° F but in the afternoon it went up to 101° F. By 6 p.m. the temperature dropped to 98° F and after that the patient had an uneventful convalescence except for a small rise of temperature to 100° F on 11-12-41. He remained normal upto his discharge on the 16th Dec.

[Such cases are not uncommon. As the text books say little about the pathological changes resulting from an electric shock we reproduce here an abstract of a paper by Alfred Weiz—Editor.]

DEATH FROM HIGH TENSION CURRENT & BRAIN DEATH

"Alfred Welz (Hanover) reports that while installing a pole for a high tension current, six men were pulling on a wire which came in contact with the high tension wire. Although the men received the same electric shock, four escaped with burns on the hands but two died. Prolonged attempt at resuscitation were without avail. The wire carried 8,700 volts with a current strength of 1 to 2 am. Necropsy showed different changes in the brains and lungs of the two men. In the first, there was a severe hemorrhagic pulmonary edema, and in the second, marked acute swelling of the brain.

Histologic examination showed plethora and acute stasis in the liver, kidneys and spleen of the first man. In addition to these changes, the brain of the second man contained extremely hyperaemic large and small cerebral vessels. The vascular sheaths of the small veins and capillaries presented unicellular and multicellular infiltrates of lymphocytes and plasma cells distributed irregularly in the form of islands all over the brain. There seemed to be no sites of predilection, although the veins of the gray substance and of the borders between the cortex and medulla appeared to be involved somewhat more frequently. In the gray substance, individual vessels showed a perivascular proliferation of glia cells. In addition to the cellular exudate, nearly all vessels showed a fresh, fluid exudation in the perivascular and pericellular spaces. Numerous other vessels presented many fibrocytes and all transitions up to complete fibrous change and thickening of the vascular sheaths. Hemosiderin crystals inside and outside the cells were observed here and there in the vascular walls. Degenerative changes in the glia cells were much less marked than the vascular changes. Calcified ganglion cells and cell destruction with neuraphagy and pseudoneuronophagy were found in places. Consequently, there were old as well as new changes in the cerebral vessels, denoting a permanent or recurring disturbance of the circulation. In the evaluation of the case, two factors must be taken into consideration: a primary damaging factor and the actual releasing factor of the fatal disturbance of circulation.

Various external and internal factors must be considered to explain why the same current killed two men while four escaped death. A current 8,700 volts and from 1 to 2 am undoubtedly endangers life, but instances of contact with a current of 15,000 volts have been reported in which a burn was the only result. The resistance of the body, the duration of the contact, the course of the current through the body and individual conditions at the time of the accident are all factors which influence the result. For instance, the four men who escaped had dropped the wire immediately, while the man in whom pulmonary edema was found at necropsy had spasmodically contracted the hands over the wire and pressed it against his chest for at least 15 seconds. The heart was located in the course of the current passing from arm to arm, and cardiac death was the result. Death from electricity is to be explained by cardiac failure. The severe pulmonary

Except in rare instances the margin of safety between the therapeutic and toxic range is sufficiently wide to enable one to avoid easily any serious reactions due to the drug itself if reasonable care is exercised. Minor complications such as skin rashes, falling hair and mild aching of the muscles, particularly those of the thigh, may be expected in approximately 10 per cent of the cases, but only infrequently will it be necessary to discontinue treatment permanently. Organic heart disease and even fairly marked degrees of renal impairment have not proved to constitute contraindications to the drug. However, it has been found that patients who have suffered a cerebral accident do not respond well to this type of therapy.

Subjective improvement as estimated by the disappearance of headaches, dizziness, tinnitus, and so on, was very definite in 63 per cent, fair in 20 per cent, and disappointing in 17 per cent. Six patients exhibited poor tolerance for cyanate as evidenced by precordial pain in 1, skin rash in 3 and skin rash combined with falling hair in 2. In addition, there were 2 other patients who felt distinctly worse while under treatment. One of these was apparently very sensitive to thiocyanate and treatment had to be abandoned because of mental confusion and physical collapse even with the blood cyanate in the accepted therapeutic range.

Some degree of reduction of the blood pressure was obtained in every case and objective results were considered satisfactory in 78 per cent, fair in 16 per cent and poor in 6 per cent. The average systolic pressure for the entire group dropped from 197 before treatment to 156 with treatment while the average diastolic pressure dropped from 115 to 94. In 4 instances the blood pressure remained normal for months or years after discontinuing thiocyanate.

The optimum blood cyanate level ranged from 4 to 16 mg per 100 cc with an average of 8.3 mg. The maintenance dose of potassium sulphocyanate varied from 3 to 21.5-grain doses per week, with an average of 9 doses per week. During the 11-year period observation 4 to 16 mg per 100 cc with an average of 8.3 mg. The maintenance dose of potassium sulphocyanate varied from 3 to 21.5-grain doses per week, with an average of 9 doses per week. During the 11-year period of observation 4 patients died of heart failure, 4 of cerebral hemorrhage, 1 of coronary occlusion and 2 of pneumonia. In no instance could death be attributed either directly or indirectly to cyanate administration. Potassium sulphocyanate is regarded by the authors as a valuable drug in the treatment of hypertension and, properly employed, capable of prolonging life and preventing disability in a substantial percentage of patients suffering from this condition. Potassium sulphocyanate can be safely administered provided proper laboratory control is exercised at all times.

The authors strongly question the conclusion expressed in a paragraph entitled 'Hypertension and the Thiocyanate' in the Journal of the American Medical Association, (p 2391 1940) and after analysing

the fatal cases, deny the implication that thiocyanate is too dangerous a drug to be used clinically, and possibly should be abandoned. No one will deny that thiocyanate is more or less toxic, but if the dose is intelligently regulated through adequate laboratory control, therapy can be extremely valuable and relatively safe.

LOW SODIUM AND HIGH AMMONIUM CHLORIDE DIET IN MENIERE'S SYNDROME

The term "syndrome" is preferable to "disease" because the exact nature of the disturbance is unknown. It typically consists of vertigo, tinnitus, deafness, nausea and vomiting, of which vertigo may be the worst. It is chronic, with acute episodes. Treatment has been of two types: (1) Surgical treatment usually consists of cutting the acoustic nerve or destroying the labyrinths and Scarpa's ganglion. Eighth nerve section usually stops vertigo but not tinnitus, therefore not only the endolymph system is at fault. (2) In medical treatment administration of low sodium-high ammonium chloride diets causes improvement.

John H. Talbott and Madelaine R. Brown (Massachusetts Gen'l Hosp JAMA 114: 125-130, Jan 13, 1940) observed 48 typical cases for periods up to three years. Most patients were 40-70 years old, about half male and half female. Blood counts, urine examinations and Hinton and Wassermann tests were negative. Thirty patients had symptoms for 1 to 20 years, usually incapacitating. Middle ear infection often preceded. Skull x-rays and lumbar punctures, when made, were negative, the caloric test was hyper or hypo-active. When previous treatment had included low sodium-high ammonium chloride diet, there was usually improvement.

Determinations of total fixed base, sodium, potassium, calcium, chloride, total carbon dioxide, phosphate, protein and non-protein nitrogen in the blood showed no consistent changes from normal. Past investigators assumed that this syndrome was associated with disturbance of water and salt metabolism—retention of sodium and a "water-logged" labyrinth. If this were correct one might expect: (1) increased sodium and fixed base with little water or protein change; (2) increased water with less sodium, base and protein; (3) decreased protein but no other changes. No such changes were observed, nor was diminution of sodium or dehydration found in patients on a low sodium diet. Attempts to induce acute attacks by water and sodium administration, resulting in increased serum pH, sodium and water concentration, decreased protein and increased carbon dioxide, led to no exacerbation.

In four patients, increased potassium and decreased sodium values were seen during acute attacks. It was found that a low sodium diet had relatively high potassium value. Since a change of potassium concentration is characteristic of familial periodic paralysis and added potassium is used in treating this as well as myasthenia gravis, a test

was made on 40 patients with Meniere's syndrome Six to ten Gm potassium chloride in water was given daily for 1 to 16 months with beneficial results Some tinnitus, vertigo and "mild attacks" persisted but comparatively normal life was possible

Theoretically potassium chloride through diuresis may increase elimination of sodium and water, also, conduction of the nerve impulse may be favoured by an optimum potassium concentration The increased serum potassium values may indicate its loss from the tissues, which thus is replenished by the added potassium No harm has resulted from a high potassium chloride diet in any case

TREATMENT OF MENIER'S DISEASE WITH HISTAMINE ADMINISTERED INTRAVENOUSLY

C H Sheldon and B T Horton (Proc Staff Meet, Mayo Clin 15 17-21, Jan 10 1940) consider the factor most probably responsible for Menier's syndrome to be a local alteration in *permeability* of the capillary wall with secondary local edema The site of the lesion is in the inner ear involving the labyrinth causing vertigo or the cochlea causing deafness Histamine is an important agent with affects capillary permeability

Fifteen patients were treated with histamine The first 4 were given subcutaneous and the next 11 intravenous injections For the latter, 19 mg histamine acid phosphate dissolved in 250 cc normal saline solution was administered intravenously in 1½ hour All patients responded in a spectacular manner Eight patients had been on ammonium chloride and potassium nitrate for several months with little or no benefit Ten patients were in the acute or subacute stages of the disease and were either partially or totally incapacitated

The drug is administered so slowly that there is no change in blood pressure or pulse rate, an occasional slight sensation of heat in the face can be avoided by controlled dosage The manner in which the drug acts is being further investigated Woltman believes that Fuustenbergs treatment, or modification, will not be displaced but that the almost immediate response to treatment with histamine makes this method valuable when vertigo is violent and vomiting severe

MECHANISM AND TREATMENT OF PREMENSTRUAL DISTRESS WITH AMMONIUM CHLORIDE

J P Greenhill and S C Freed (Loyola Univ, Chicago Endocrinology 26 529-531, March, 1940) have postulated a single mechanism for the development of the variety of changes which occur premenstrually The development of premenstrual distress is according to this hypothesis, the result of sodium ion retention by the different tissues of the body under the influence of the ovarian steroids This retention of sodium is associated with an increase in extracellular fluid in the tissue which may be microscopic in amount

or may develop into gross edema. The neurologic symptoms, under this theory, result from edema of the nervous system, probably the brain, the nausea and bloating of the abdomen result from edema of the gut, and the other symptoms arise from the specific organs affected.

Actual proof of this working hypothesis is lacking, although many physiologic reactions can be presented as support for these conclusions. For instance, sex hormones are steroids which have a definite effect on water balance. Estrogens, androgens, progesterone and other hormones are capable of causing sodium ion retention. On the basis of the hypothesis that premenstrual distress results from tissue edema, the authors attempted to institute therapy whereby the excess sodium and associated fluid are withdrawn. For this purpose, ammonium chloride was administered by mouth.

Fifteen patients were treated who were apparently normal except for development of marked premenstrual distress. In several, a diagnosis of premenstrual tension would be permissible, so severe were their symptoms. Two patients had marked edema of the legs and face and two had vulvar edema to the extent that they were unable to wear underclothing in comfort during the premenstruum.

The patients were advised to refrain from adding table salt to their food during the last two weeks of the menstrual cycle. They were given at this time 0.6 Gm. ammonium chloride three times daily.

Treatment was uniformly successful. All the patients were highly gratified with the therapy. Gross edema did not occur in the patients who had previously demonstrated it. Distention of the abdomen, nausea and migraine were absent or insignificant during therapy. The patients claimed that they were less irritable and not subject to the periodic emotional upsets. All patients stated that there was an improved sense of well-being.

This therapy had no effect on two women who had migraine which did not occur at the premenstrual period. Patients with dysmenorrhea and painful breasts were likewise not relieved. The beneficial results were not permanent but were obtained only so long as the ammonium chloride therapy was maintained.

TREATMENT OF MIGRAINE WITH INTRAMUSCULAR INJECTIONS OF METRAZOL

A. Leroy (Liege) states that the variety of theories advanced to explain the pathogenesis of migraine accounts for the diversity of treatments for the disorder. Among others, ergotamine tartrate, acetylcholine and pituitary extracts have been recommended as giving good results. Most investigators attribute a primary importance in the pathogenesis and treatment of migraine to the changes in composition of the blood, and this led Leroy to use shock

treatment (intramuscular injections of 10 per cent metrazol in doses of 0.25 to 0.40 Gm.)

He cites three cases of severe migraine in which he has used metrazol. The first patient had attacks of migraine for 50 years. He was given 17 injections (0.2-0.3 Gm each) of metrazol in four months, and his attacks, which used to recur every 10 days, then appeared after one month and consisted only of slight headache, at times followed by vomiting. The second patient had had attacks of migraine for five years. He was given four injections (0.2-0.5 Gm each) of metrazol and was completely relieved. The third patient is a neurasthenic who had had migraine for one year. He was given 15 small injections (0.1-0.25 Gm each) of metrazol and was relieved and satisfied.

The administration of 0.25 to 0.3 Gm metrazol between attacks has abolished migraine rather rapidly even in cases of long standing. At times, the injection is followed shortly by an attenuated attack and in some cases by diarrhoea.

C. Pfeiffer has used potassium chloride and calcium lactate 10 grains of each, twice to four times a day, with most satisfactory results. The use of these drugs with low sodium and high ammonium chloride diet has proved satisfactory in a number of spasmodic conditions of allergic origin.

Book Reviews and Notices

DISEASES OF THE NERVOUS SYSTEM Described for practitioners and students 2nd ed By F M R WALSHE, M.O., D.Sc., F.R.C.P., published by E & S Livingstone, Edinburgh, 1941, pp 325, price 12s 6d

Most practitioners and students of medicine consider neurology a difficult subject and neglect its study. The practitioner is obsessed with the idea that as most of the nervous diseases are incurable, it is not his worthwhile to diagnose them. The trouble, he thinks, is too much. We consider this to be a wrong view. The diagnosis of nervous diseases, if the patient is studied systematically, can be very easy, and as to treatment, neurology offers just as much scope for the resourceful practitioners as any other branch of clinical medicine. The only difference is that the persons suffering from the incurable diseases of cardiovascular, renal, and other systems do not live so long as the sufferers of nervous maladies!

Dr Walshe has written an ideal introduction to Neurology. The treatment is simple, lucid and the language is incisive and easy to read. It is a pleasure to come across beautiful world pictures and caustic Irish wit in a medical text book. The book is divided in two parts, the first deals with general principles of neurological diagnosis, and the second gives a descriptive account of the more common diseases of the nervous system. His exposition of the production, and interpretation of nervous symptoms based on physiological principles is clear and illuminating, the descriptions of diseases are lucid and the clinical word pictures of diseases, emphasizing the time factor in explaining the variations in symptomology, are excellent. His descriptions of Disseminated Sclerosis and Parkinson's disease are models of clinical writing. The outlook throughout the book is thoroughly practical, and though at places dogmatic the dogmatism is born of a wide clinical experience and a sound physiological training.

Some neurological diseases are not so common in India as they are in Europe. Disseminated Sclerosis in Bombay at least is rare, one hardly sees a case or two in a year, while the disease is extremely common in Europe. But we have enough of vascular disorders of the nervous system, syphilis of the nervous system, myopathies, motor neurone diseases, tumors, and degenerations. There is no excuse for any student or practitioner to be not acquainted with the modern methods of diagnosis and treatment of nervous diseases. To such there can be no better introductory book than Dr Walshe's manual.

BIOLOGY IN THE MAKING By Emily Eveleth Snyder, McGraw-Hill Book Company Inc New York and London pp 539, price 18s

This is one of those books for general readers for which we can justly say that we were waiting for a long time

The Science of biology is one of the basic Sciences Without a sound grasp of its principles, it is impossible to follow modern thought Medicine psychology, philosophy, politics, economics are really aspects of human biology and, if pursued divorced from its parent biology are likely to produce misleading and fantastic results And that is what is unhappily happening all over the world at present One longs for a time when biology will be a compulsory study for every citizen

In medicine at least the study of biology is in the curriculum for the first year Unfortunately the approach is superficial and the student instead of making biology the foundation on which to build his future work, considers it a mere incidence in his medical studies to be skipped over as best as he can, and be forgotten forever afterwards

In medicine at least the study of biology is in the curriculum for development of biological discoveries not as so many facts, but as the product of real men whose lives, for one reason or another, made them outstanding in their fields Pictures of many scientists, ranging from Aristotle to Alexis Carrel are presented and at the end of every chapter for the readers wishing to follow further, the work of a particular scientist or development in a particular field, suggested readings are included A complete bibliography and a list of scientists from Hippocrates (460-3593 cc) to Lindbergh (1902) and Stanley (1904) together with their dates of birth, death, country and major contributions are given

The language is simple, lucid and telling The chapter headings themselves are arresting

We confess that Snyder's presentation of the history of biology through the personality of its chief workers and through its contact with man in the prevention and cure of disease and through its effect on agriculture and horticulture is so thrilling that we could not put the book down till we had read it right through, to the last page We are certain that any reader who takes it up will find it as thrilling as a romance or a detective tale Every schoolboy in his last school year, every student of biology, every medical student when reading physiology and pathology and every physician, who we believe is or is a biologist and a naturalist par excellence, should read this book It cannot fail to fire the young with enthusiasm, and make the others feel that people who talk about science as the cause of all the present ills of mankind are talking unmitigated nonsense As long as men are curious about themselves and other living organisms, as long as they want to improve their crops and herds, as long as they desire to prevent and cure disease, the study of Biology is a necessity and an exciting adventure No better book can be found than *Biology in the Making* to interest the lay reader as well as the student of the subject

The Indian Physician

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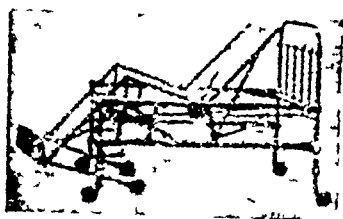
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Let us remember....

PARACELSUS

Theophrastus Bombastus Von Hohenheim

(1493-1541)

A Destructive Genius of the Renaissance



A contemporary of Jean Fernal, Theophrastus Bombastus Von Hohenheim—the epithet Paracelsus was of his making, added on his family name to show his superiority to Celsus—was entirely a different personality. He was born at Einsiedeln, Switzerland, in 1493, and died on the 24th September, 1541, at Salzburg. The cause of his death is not known, his enemies asserted that he died in a low tavern in consequence of a drunken debauch, while his friends maintained that he

was thrown down a steep place by some agents of either physicians or apothecaries whom he had harassed all his life

The reputation that Paracelsus built up in this short space of 48 years is a most baffling one. On one side he was considered to be a boastful, uneducated charlatan, an egoistic noise-maker, a drunken biaggait, a devil worshipper, an eccentric fool, a zealous halfwit, a superstitious visionary, a megalomaniac! On the other hand he acquired a just reputation as a successful physician, and was acclaimed a medical Luther, and a medical pathfinder.

Sudhoff who edited the authentic works of Paracelsus in fifteen big volumes, showed that upto 1658 not less than 390 editions, reprints and translations appeared of his writings. His mysticism has appealed to many and in 1936, the Deutsche Volkshelbewegung, patronized by the Nazis, demanded the reversal of the present healing art according to the concepts of Paracelsus! Goethe and Browning were attracted by him. He appealed to them as a symbol of the deep yearning of humanity. The greatness of his strife for the highest spiritual attainments and the tragedy of the short-coming of an indefatigable will against the unattainable, have a compelling attraction for all romantic searchers after truth.

He studied alchemy from his father, who was an alchemist and a physician. He joined the University of Basel at the age of sixteen but soon left it to study chemistry from Trithemius the abbot of Sponheim and afterwards of Wurzburg, who was an alchemist of repute at the time. But the fiery spirit of Paracelsus was not satisfied by the search for the philosophers' Stone and he left the study of school chemistry as he had forsaken University culture, and went to work in the mines in Tyrol.

The sort of knowledge he got there pleased him much more. There at least he was in contact with reality. The struggle with nature before the precious metals could be made of use impressed upon him more and more the importance of actual personal observation. He saw all the mechanical difficulties that had to be overcome in mining, he learned the nature and succession of rocks, the physical properties of minerals, ores and metals, he got a notion of mineral waters, he was an eye witness of the accidents which befell the miners, and studied the diseases which attacked them, he had proof that positive knowledge of nature was not to be got in schools and universities but only by going to nature herself.

and to those who were constantly engaged with her Here came Paracelsus's peculiar mode of study He attached no value to mere scholarship Scholastic disputations he utterly ignored and despised He went wandering over a great part of Europe to learn all that he could In so doing, he was one of the first physicians of modern times to profit by a mode of study which is now reckoned indispensable The book of nature, he affirmed, is that which the physician must read, and to do so he must walk over the leaves

On his return to Basel from his wanderings in 1526, he was appointed town physician and lecturer of medicine at the Basel University He had acquired a rich store of facts during his wandering period of ten years His lectures on medicine broke away from tradition They were in German, not Latin, they were expositions of his own experience, of his own views, of his own methods of curing adapted to the diseases that afflicted the Germans in the year 1527, and they were not commentaries on the text of Galen or Avicenna They attacked not only the great authorities of the past, but criticized in no measured terms the current medicine of the time, and exposed the practical ignorance, the pomposity, and the greed of those who practised it He began his lectures by publicly burning the books of Galen and Avicenne, and crying "Ye Avicenna, Galen, Rhazes, ye Suevra, Vienna, Cologne, ye Italy, Greece, Arabia, Israelite, after me, not I after you, the time will come when all of you will be a Contempt of the world Mine will be the monarchy!"

The truth of Paracelsus's doctrines was confirmed by his success with patients From all parts of Europe persons of high rank sought his help in severe cases He apparently had that God-given faculty of an intuitive therapist combined with broad practical knowledge He had high ethical standards He vowed

"I shall never cede from my medical work as long as God favours me with his mission I shall oppose all false medicine and teachings I shall love the sick more than myself, not take recompense that I do not deserve I shall advise the careworn, look after the melancholic"

A recent leader writer in the Journal of the A M A states "He openly admitted that he was 'not always capable of giving at once an opinion, such was customarily pretended only by the

"humoral" physicians If anybody, it was he who treated the diseased individual, yet he composed objective descriptions of particular diseases e.g., hospital gangrene, of syphilis in its variability, its infectiousness and its heritability, of the tartaric, i.e., the stone diseases, which he explained as the effect of precipitations as he observed them in his chemical experiments, of cretinism due to goiter in the parents, of miner's diseases (independently of his contemporary Agricola), St Vitus's dance, St Anthony's fire, mental diseases he declared were caused not by any saints or demons but by natural influences 'Local decay or decay of the organs of expulsion generate disease' Psychic therapy he consciously applied 'There are physicians who have the power to overcome diseases by their will power' In surgery he approached the aseptic ideal 'Keep the wounds clean, probe, cut, saw as little as possible and they will heal' His '*Grosse Wundarzeny*' is mostly concerned with avoiding operation His laboratory activity raised alchemy to chemistry Alchemy is to make neither gold nor silver but the supreme essences and to direct them against diseases He propagated the application of minerals Nothing is a poison in itself, all depends on the proper preparation, dosage and indication To ascribe character, sickness and other destinies to the influence of heavenly bodies he regarded as superstition, a ridiculous tale of astrologers The course of Saturn lengthens or shortens nobody's life, a child owes nothing to star constellations but all to his parents All this was progressive and to us seems good and reasonable But in his time it was rebellion against the dogmas in medicine which the doctors had to follow strictly "

All this frank rationalism aroused bitter opposition His enemies asked for his degrees, for the proof of his qualifications The apothecaries attacked him because he had his own pharmaceutical system and had set the authorities against them with regards the purity of their preparations The growing jealousy and enmity drove him from Basel and he took to wandering again He seldom stayed more than a twelve-month in any one place and had often to leave place after place from absolute want The course of his wanderings of some twelve years can be traced by the dates of his various writings In 1541, the Archbishop of Ernst invited him to settle at Salzburg under his protection, where he soon "exchanged life for death" in his forty-eighth year.

It will serve no purpose to delve deeply into the medical doctrines of Paracelsus. Their influence has entirely passed away and they are of interest only for their place in a general history of medicine and philosophy. The peculiar method of Paracelsus, which perhaps is the method of all mystics, can best be described in the words of the medical historian Cumston: "For Paracelsus, the method of acquiring knowledge was a kind of theosophical intuition by means of which he said that man should come into intimate contact with God and all created things. In his intuition there is a mystic light which reaches all things to the human mind and gives it the strength to drive away demons, by it one communicates with God from whom all things are received, because man creates nothing. This process of intuition developed by Paracelsus was a fundamental principle of the gnostic philosophy of the Alexandrian school of the sixteenth century. According to Paracelsus a man who renounces all sensuality, and blindly obeys the will of God will be able to identify himself with the acts of the Celestial reason and thus will possess the philosophers' Stone."

"We may say at once that the glory of Paracelsus is a result rather of his genius than of his destructive brutality, for the edifice built by Hippocrates and Galen still remains almost intact in spite of his attacks upon it, while the building of which he himself laid the foundation has endured through centuries and is added to every day. He sowed the first seeds of medical chemistry, which had no existence before him, he strongly advocated the use of antimony, iron, lead, arsenic and mercury—the specific for syphilis—which still survives, and will probably exist for a long time to come as the last trench of empiricism to be taken.

"Paracelsus tells us that experience has shown that mercury is the sovereign and only remedy for the cure of all ulcers tainted with the great pox. Sublimated mercury has been retained in this business as a general remedy because its great virtue has been known to everybody. It is given by mouth, and cures by inducing abundant expectoration of saliva, not because the saliva is the cause of the disease but because it is mixed with it.

"Paracelsus also referred to the extraction of the quintessence of plants, but this was only accomplished at the beginning of the nineteenth century when P. J. Pelletier and his

collaborator, Caventou, prepared sulphate of quinine and afterwards proceeded to the extraction of vegetable alkaloids

"Paracelsus even foresaw the practice of asepsis, for he says Do not touch wounds, as they cure themselves, it is the external agents which militate against the process of cicatrization He inaugurated an ingenious diagnostic method still used to-day for the diagnosis of indefinite syphilitic manifestations, and he affirmed that by the nature of the remedy one might determine the nature of the disease Although it must be admitted that the mental equilibrium of Paracelsus was far from perfect, he certainly gave a great impetus to the progress of medicine He was led astray by his love for the occult sciences, delved deep in the Arcana and dallied with researches for the discovery of mysterious panaceas complicated with astral influences, but on the other hand he foresaw with marvellous lucidity of intelligence explanations of things still hidden in obscurity As he says Before the end of the world a large number of supernatural things will be explained by physical causes"

Original Contributions

LINEAR MEASUREMENTS OF THE HEART IN CASES OF HYPERTENSIVE HEART DISEASE

By RUSTOM J VAKIL,

M D (LOND), M P C P (LOND) D T M & H (LOND) F R F I S G, I P
BOMBAY

*(Working with the aid of a medical research grant from the Trustees of
the late Sir Ratan Tata)*

A correct measurement of the size of the heart has been the goal of all cardiologists. The subject of heart-size has evoked considerable enthusiasm in medical circles, and has been the subject of innumerable papers and investigations. Determination of apex beat by inspection or palpation and mapping out of cardiac borders by the method of percussion do furnish us with some sort of information about the size of the heart, but there is no doubt that for more exact information we have to depend upon radiology. Two main methods of X-ray projection have been employed in the estimation of heart-size, viz., orthodiography and teleradiography (or tele-roentgenography). Though from the point of view of accuracy, there is not much to choose between the two methods, the majority of present day authors are inclined to regard orthodiography as more convenient and reliable.

For many years, the subject of cardiac mensuration was pursued with great zeal by cardiologists and radiologists and much credence paid to the various measurements. The last few years have however witnessed a change in medical opinion, a tendency on the part of specialists in the field to doubt the value of cardiac mensuration, the subject of heart-measurement which, at present, is in the melting pot may, who knows sink into obliquity in years to come.

Since the blood content of the heart accounts for practically 50% of the total cardiac bulk, the question has often been raised

whether the amount of blood present in the heart at the time of measurement may not affect the accuracy of our measurement. Workers, who incline to this view, are apt to regard cardiac mensuration as a grossly inaccurate and unnecessary form of investigation. It has been convincingly demonstrated of late by several observers that the "diastolic volume" of the heart and "the mass of blood in the heart in diastole" are fairly constant factors in any given individual. In view of this fact, we are inclined to regard cardiac mensuration as a fairly accurate and useful form of investigation applicable to the study of heart disease, coupled with clinical examination of the heart, it is likely to afford valuable information about the heart, taken singly, it is of no value and likely to prejudice the examiner. This is true not only of cardiac mensuration but also of other lines of investigation like electrocardiography and sphygmography.

According to Eyster, early detection of cardiac enlargement by roentgenological methods is "the most important single factor in determining the presence or absence of organic heart disease." It should be noted, however, that in the early stages of ventricular hypertrophy, cardiac enlargement may not be detectable during life, even by the "precision methods" of today, in Paul White's opinion, hypertrophy of cardiac muscle to the extent of 25 or 50 g in weight may be missed even by an expert radiologist, such degrees of hypertrophy being obvious only in the post-mortem room. Much has been written in recent years on the radiological detection of early enlargement of the heart and aorta in cases of rheumatic heart disease and syphilitic aortitis. Though a similar interest has been shown by medical circles in the subject of hypertensive heart disease from the clinical point of view, the radiological side of the question has not received its just share of attention. It was with a view to gain further insight into the radiological problems associated with hypertensive heart failure that the present investigation was undertaken. The varied appearances of the lung-fields and cardiac silhouettes in cases of hypertensive heart disease have been already dealt with in a previous paper (Vakil, R. J. "Radiological Appearances of the Heart and Lungs in cases of Hypertensive Heart Failure" *Ind Med Gazette* LXXV No. 7 July, 1940). The purpose of the present paper is to deal not with alterations in shape but alterations

great vessel shadows on the right border of the cardiac silhouette (point A) to the point of the cardiac apex (point B)

T D, the *transverse diameter* or the "*horizontal diameter of Bordet*" (CD+EF) is measured by adding the maximal distance of the right cardiac border from the mid-sternal line (line CD) to the maximal distance of the left border from the same mid-sternal line (line EF)

B D, or the *broad diameter* of the heart represents the sum of the lengths of two perpendiculars dropped on the line of the long diameter (line AB), one (line JK) from the junction of the pulmonary conus with the left ventricular border (point K) and the other (line GH) from the junction of the right lower cardiac border with the diaphragm (point G)

The *diameter of the right auricle* (line AG) represents the distance between the right cardio-vascular junction (point A) and the right cardio-hepatic angle (point G)

The *diameter of the left auricle* (line LK) represents the distance of the left cardio-vascular junction (point K) from the mid-sternal line

The *diameter of the right ventricle* or the "*right ventricular chord*" (line GB) represents the distance between the right cardio-hepatic angle (point G) and the point of the cardiac apex (point B)

The *diameter of the left ventricle* or the "*left ventricular chord*" (line KB) represents the distance between the left cardio-vascular junction (point K) and the point of the cardiac apex (point B)

The *bisector* (line MN) represents the maximum distance of the left ventricular border from the left ventricular chord (line KB)

The *right medium diameter* (line CD) represents the maximum distance between the right cardiac border and the mid-sternal line

The *left medium diameter* (line EF) represents the maximum distance between the left cardiac border and the mid-sternal line

The *angle of inclination* (angle SRB) of the heart represents the angle between the long diameter of the heart (line ARB) and the horizontal (line RS)

The cardio-thoracic or the heart-lung coefficient is the ratio between the transverse diameter of the heart (CD+EF) and the widest diameter of the chest

The width of the great vessels (line PQ) represents the distance between the right and left borders of the vascular pedicle at the level of its widest part

The abovementioned measurements, as estimated in the present series of cases, are set out in Table I Table II besides giving average, maximal and minimal values for the different measurements in the present series of cases, gives corresponding values in normal subjects for comparison

TABLE I
Measurements of the Heart in 35 cases of hypertensive failure
(measurements in cms except when stated)

Serial Number	Longitudinal Diameter	Transverse Diameter	Broad Diameter	Diameter of Right Auricle	Diameter of Left Auricle	Diameter of Right Ventricle	Diameter of Left Ventricle	Bisector	Right median	Left median	Angle of Inclination	Cardio-thoracic Ratio	Width of the great Vessels
1	16.8	14.8	11.2	7.5	4.8	14.8	11.0	0.6	4.6	10.2	30	48%	7.7
2	14.8	13.4	10.1	6.4	3.4	13.4	10.1	0.6	4.6	8.6	34	40	6.8
3	13.8	12.4	10.8	6.5	3.9	12.3	10.5	0.5	3.6	8.8	32	46	5.4
4	15.6	14.2	11.2	7.2	5.4	14.4	10.4	0.8	4.1	10.1	38	59	4.9
5	15.4	15.0	11.1	6.2	3.9	15.5	11.8	0.7	4.9	10.1	33	56	7.9
6	16.3	16.2	11.0	7.5	4.1	16.0	9.6	1.0	5.8	10.4	27	55	7.3
7	21.0	21.6	12.7	8.0	7.2	20.8	10.0	1.4	8.6	13.0	28	65	12.6
8	15.1	13.9	10.4	6.6	4.1	14.3	10.9	0.7	4.3	9.6	38	57	4.8
9	14.3	11.9	9.7	7.7	3.8	11.3	9.8	1.1	3.7	8.2	38	45	7.1
10	13.3	13.6	10.1	7.3	3.6	11.7	8.4	1.6	3.6	10.0	17	48	7.2
11	12.5	12.1	9.4	6.3	3.4	11.8	8.2	1.6	3.4	8.7	29	44	6.5
12	12.8	12.1	10.1	6.8	4.8	11.6	8.3	0.8	3.3	8.8	33	43	7.2
13	14.7	15.0	11.5	8.6	3.4	13.1	9.8	2.6	4.8	10.2	23	53	7.5
14	14.6	13.4	12.2	8.7	3.5	12.8	9.8	1.2	4.8	8.6	33	48	7.1
15	12.8	11.6	8.8	7.0	2.9	10.8	8.4	1.2	3.2	8.4	25	42	6.4
16	14.9	14.4	9.6	7.7	3.3	11.8	9.2	1.8	4.6	9.8	25	48	7.1
17	14.0	14.5	11.2	8.8	3.6	11.6	9.5	2.7	4.6	9.9	22	51	6.6
18	14.3	14.0	9.1	7.6	3.8	11.2	8.6	3.4	4.5	9.5	29	58	5.9
19	12.9	12.5	9.2	6.8	3.6	10.7	8.5	2.4	4.0	8.5	27	54	5.3
20	14.0	12.2	10.5	7.1	3.7	11.2	11.0	1.4	4.3	7.9	44	41	6.4
21	13.3	11.5	10.0	7.0	3.8	11.0	9.0	1.6	3.3	8.2	35	46	6.8
22	12.2	11.6	11.4	7.2	3.6	9.4	10.8	2.6	4.3	7.3	35	43	6.7
23	13.5	11.5	11.2	6.7	4.4	11.0	10.8	1.4	4.2	7.3	44	40	6.7
24	13.4	11.6	9.2	6.3	5.2	11.0	8.6	1.7	2.9	8.7	39	50	6.3
25	12.1	10.5	10.1	7.2	5.2	9.0	8.4	1.6	3.1	7.4	48	48	7.2
26	14.9	12.8	10.0	8.0	5.3	11.5	8.8	2.0	3.2	8.6	41	52	5.1
27	15.4	14.5	11.3	8.3	5.5	12.6	9.5	2.7	4.2	10.2	44	53	7.4
28	16.1	13.6	10.7	8.0	5.4	12.7	9.8	2.3	4.2	9.4	47	X	7.6
29	13.9	13.0	10.4	8.7	7.0	11.4	9.2	2.0	3.8	9.2	44	53	5.5
30	13.7	13.2	11.7	7.6	4.0	11.0	11.8	2.6	3.6	9.6	32	56	5.4
31	15.3	14.5	11.2	8.7	4.9	11.8	9.5	2.8	4.7	9.8	34	50	10.4
32	13.7	11.3	9.2	7.1	4.5	10.1	8.8	1.3	3.5	7.8	44	48	4.7
33	14.3	12.2	9.6	6.7	3.6	10.9	9.7	2.0	3.8	8.4	42	50	5.2
34	15.3	13.1	9.9	7.0	4.7	13.1	9.4	1.0	4.3	8.8	42	54	6.7
35	12.9	11.1	10.0	7.9	4.8	8.9	8.4	1.9	3.3	7.8	46	50	5.8

TABLE II
Average, maximal and minimal values

Cardiac Measurement	Present Series of cases			Normal 1 ig		Compiled from different authors
	Average	Maximal	Minimal	Average	Maximal	Minimal
1 Long diameter	14 4	21 0	12 1	13 6	15 5	11 0
2 Transverse diameter	13 3	21 6	10 5	12 2	14 5	9 2
3 Broad diameter	10 4	12 7	8 6	9 8	11 2	8 0
4 Diameter of right auricle	7 4	8 8	6 2	5 0	6 5	3 5
5 Diameter of left auricle	4 0	7 2	2 9	4 2	5 0	3 5
6 Diameter of right ventricle	12 1	20 8	8 0	11 4	14 7	8 5
7 Diameter of left ventricle	9 6	11 8	8 2	9 6	12 5	6 6
8 Bisector	1 7	3 4	0 5	1 2	2 0	0 6
9 Right median diameter	1 2	8 6	2 9			
10 Left median diameter	9 1	13 0	7 3			
11 The angle of inclination	35°	48°	17°	43°	57°	20°
12 Cardio thoracic ratio	50%	65%	40%	49 50%	57%	36%
13 Width of great vessels	6 7	12 6	4 7	6 0	7 0	5 0
14 Right median Left median	1 2 17	1 3 0	1 1 5	1 1 92	1 2 2	1 1 7
15 Long diameter Transverse diameter	11 10			11 10		

Results

A study of Tables I and II allows us to arrive at the following conclusions with regard to the measurements of the heart in cases of hypertensive heart failure —

(1) Practically all the linear measurements of the heart display a wider range of figures in hypertensive heart disease than in normal subjects

(2) The three main diameters of the heart, (viz, the long diameter, the transverse diameter and the broad diameter) show a proportionate increase in cases of hypertensive failure, as a result, the ratio of the long diameter to the transverse diameter is unaltered

(3) There is little or no increase in the size of the left ventricular chord (the so called "diameter of the left ventricle") This is strange, in view of the fact that the first chamber of the heart to hypertrophy or dilate in cases of high blood pressure is obviously the left ventricle, hence, it appears that the left ventricular chord is of little or no value as guide to the size of the left ventricle The bisector is a far more useful measurement than the left ventricular chord in assessing the degree of left ventricular hypertrophy in cases of hypertension

(4) Another surprising feature noted is the lack of alteration in the average value of the cardio-thoracic ratio With enlargement of the heart, one would have expected an increment in this value

Summary

(1) The present paper presents a study of the various measurements and diameters of the heart in cases of hypertensive heart failure. 35 cases have been orthodiographically studied for the purpose of this investigation.

(2) Normal measurements of the heart, worked out by competent authorities elsewhere, are presented for the sake of comparison.

(3) Deviations from normal are discussed. The futility of regarding the left ventricular chord as a measurement of the size of the left ventricle is demonstrated, the bisector is suggested in its place as a more useful measurement of left ventricular hypertrophy.

OBSERVATIONS ON PELLAGRA IN BOMBAY

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Nutritional anaemia is extremely common in Bombay. There is no statistical study of the subject, but we feel that a large number of the patients who seek hospitalization suffer from nutritional anaemia, and in the outpatient department of the general hospitals perhaps anaemia is the most frequent manifestation. Of these patients suffering from anaemia some show pellagra-like symptoms. Pellagra in its classic form is not endemic in Bombay. There is no survey made of its incidence in various parts of India and we cannot say to what extent it exists in those parts of India, such as Dohad, the Panch Mahals and South Rajputana, where maize is a staple diet, at least among the Bhils. An inquiry into this is badly needed and we hope that if not the Government, the social workers or the medical practitioners in these areas will make such a survey.

In Bombay we occasionally meet patients with pellagra. We have notes of such ten patients treated by us recently in the Bhatia General Hospital. The interest of these cases lies in the fact that they were all high class hindus, strict vegetarians, belonging to a fairly high social and financial status in Bombay compared with the patients attending the out-patient departments of the general hospitals.

Case 1. A female Hindu patient aged 40, was admitted to the Bhatia General Hospital in May 1940, for weakness of about 2 months' duration, frequency of stools about 3 per day and repeated attacks of sore tongue. On examination she was found to have brownish pigmentation on the neck, dorsum of the hands and feet and the elbow, and *perles* at the corners of the mouth. There were no neurological signs. The heart and lungs were normal. The blood count showed red blood cells 4,200,000 per cmm, white blood cells 5400 per cmm and Hb 70 per cent. She was put on the injections of nicotinic acid 100 mgm per day, and liver extract 5 c.c daily and 300 mgm of

nicotinic acid and 60 grains of ferri et ammonium citras per day. Her diet in the hospital consisted of 3 pints of milk, 5 mangoes and 4 bananas per day. She made a steady recovery in a month increasing her weight from 115½ lbs to 126 lbs.

Case 2. A female Hindu patient aged 19 was admitted to the hospital in Nov-'40 with the complaint of stomatitis and frequency of stools for the last three months. On examination she had brownish pigmentation on the dorsum of the hands and feet, there were no changes in the CNS, the heart and lungs were normal, liver and spleen were not palpable. Her blood showed red blood cells 3,200,000 per cmm, Hb 62 per cent, and white blood cells 9900 per cmm. She was put on milk diet, bananas and injection of liver extract 2 cc daily and an oral administration of nicotinic acid 300 mgm per day and iron mixture. She was discharged cured, with an increase of weight from 101 lbs to 114 lbs.

Case 3. A Hindu lady aged 50, was admitted in October 1940, with the history of weakness and pigmentation of hands and feet for the last 4 months. This was her second attack, she had a similar trouble in 1939. She was again admitted for the third time in June 1941 for the same trouble. Her blood showed red blood cells 3,600,000 per cmm, Hb 60 per cent, and white blood cells 9900 per cmm. She was on the usual routine treatment, and she was discharged with marked benefit with an increase in weight from 75 lbs to 82 lbs.

Case 4. A Hindu male aged 44, was admitted to the hospital for frequency of stools and glossitis for the last 3 months. He had oedema of the feet and signs of free fluid in the abdomen. His finer nails were typical spoon-shaped. The extensor surfaces of the arm and hands and legs showed brownish pigmentation with some scaling. Liver and spleen were not palpable, heart, lungs and CNS were normal. The blood examination showed Hb 40 per cent, red blood cells 2,200,000 and white blood cells 7200 per cmm. Gastric juice showed complete achlorhydria, Kahn reaction was negative. He was treated on the usual lines and he showed steady improvement.

Case 5. A Hindu female aged 32, was admitted for weakness, dyspepsia, frequency of stools about 3-4 per day and sleeplessness for five months. She had pigmentation of the feet and face. There were signs of free fluid in the abdomen. The blood showed Hb 22 per cent, red blood cells 1,200,000 per cmm, and white blood cells 3400 per cmm. She was treated on the usual lines and showed considerable improvement.

Case 6. A male aged 24, was admitted to the hospital for diarrhoea, glossitis and dermatitis for the last 2 years. There was typical pigmentation and dermatitis. Liver and spleen were not palpable, heart, lungs, and CNS showed no abnormality. The blood examination showed Hb 70 per cent, red blood cells 3,800,000 per cmm and white

blood cells 7,000 per c mm , B P 95/60 He was put on the usual line of treatment and increased in weight from 86 lbs to 110 lbs

Case 7 A female aged 40, was admitted for weakness, mental cloudiness, and sore tongue for the last few months She had pigmentation on the dorsum of hands and *small warty yellow excrescences* on the nose and the naso-labial folds Heart, lungs, and C N S were normal Liver and spleen were not palpable The blood showed red blood cells 3.2 million Hb 60 per cent and white blood cells 8700 per c mm She increased in weight from 67 lbs to 78 lbs and the small excrescences disappeared from her face on the usual line of treatment

Case 8 A male aged 24, was admitted for diarrhea for the last 3 years and severe stomatitis He had typical pigmentation and dermatitis on the limbs. Heart, CNS and lungs were normal, liver and spleen were not palpable The blood picture showed red blood cells 2.5 million Hb 52 per cent and white blood cells 2400 per c mm He improved on the usual line of treatment

Case 9 A male aged 26, was admitted for sore tongue, diarrhoea, and pigmentation of the hands and face for the last 3 months Heart CNS and lungs were normal Liver and spleen were not palpable The blood showed 70 per cent Hb red blood cells 3,100,000 per c mm and white blood cells 4800 per c mm In the wards he developed arthritis of wrist and small joints Kahn reaction was negative Urine examination and prostatic massage were negative He improved on the usual treatment

Case 10 A female Hindu aged 32, had severe stomatitis, diarrhoea, pigmentation and dermatitis of the hands and feet and marked psychotic symptoms Her blood count showed red blood cells 2.1 million per c mm Hb 35 per cent and white blood cells 5500 per c mm She was put on 500 mgm of nicotinic acid per day, a liberal diet of milk and bananas and made a rapid recovery Her weight steadily increased from 88 lbs to 110 lbs

Of these 10 patients 6 were females and 4 males All suffered from (a) glossitis, (b) gastro-intestinal symptoms, -anorexia and diarrhea, (c) anaemia (d) dermatitis or pigmentation Only two patients had mental symptoms Gastric juice was not examined, except in one patient who showed achlorhydria The duration of symptoms in all was for several months before medical advice was sought A detailed neurological examination is not recorded in the notes but all had complained of paraesthesia, burning sensations, and vague pains in the muscles One patient showed interesting skin excrescences which are worth noting in detail These were warty growths

of dirty yellow colour round about the naso-labial folds and on the nose. At first they appeared like collection of dirt but it was not possible to remove them by washing or by cleaning with spirit. They were most probably produced by the obstruction of the sebaceous ducts, producing the peculiar sulphur flaked appearance of the skin.

The diet on which these patients subsisted before they developed pellagra-like symptoms was the same as that of the other members of the family, and it was not possible to draw any definite conclusion that the diet was specially poor in the P-P factor.

Classical pellagra is a clinical syndrome. Its diagnosis is also a clinical one. There is no laboratory test to confirm or refute the diagnosis which is made by observing the characteristic glossitis, the gastro-intestinal symptoms, the typical dermatitis, the neurological and psychotic symptoms. Pellagra attacks all strata of society, all races and both sexes. Spies has suggested that pellagra in many persons actually begins early in childhood. It will be interesting to examine the children in the pellagra families and follow them up to note if they show any evidence of pellagra, beriberi, or riboflavine deficiency later on.

In the pellagrins there is a long history of gastro-intestinal disturbance. Loss of appetite is the first symptom. It is followed by burning of the tongue especially the tips and the sides. Later there is a frank glossitis, the typical red raw smooth tongue. There may be multiple ulcers and the ulceration may spread to the pharynx, oesophagus, gums, or lips. Enteritis with diarrhea or in some cases constipation is present. In some cases there is severe proctitis with foul diarrhea. Abdominal distention and pain are frequent. The mucous membrane of the stomach is said to show fiery red ulcers on gastroscopic examination and the mucous membrane of the genito-urinary tract is also affected in severe cases, resulting in urethritis, vaginitis and endocervicitis. Achylia is said to occur in 60% of the cases.

The skin lesions are typical and diagnostic. The skin is rough, scaly, erythematous, cracked and sharply demarcated from the healthy skin. The lesions are bilaterally symmetrical and appear on the dorsum of the hand, elbow, feet, ankles, the neck

and the face. The axilla, the perineum and the scrotum or vulva may be affected. There is marked pigmentation in the older lesions. The skin condition is constantly changing, presenting variable appearance from time to time. The marked erythematous patches or typical rosary round the neck of the western writers is rarely seen in Bombay, where thickened dark pigmented patches on the exposed parts of the body are the most frequent.

Nervous and mental symptoms are common in the classical pellagra. In our patients nervous signs were not observed in any, and only two had psychosis. These two showed marked improvement after administration of nicotinic acid and within forty-eight hours all mental symptoms had disappeared.

A well balanced high calorie diet and nicotinic acid, nicotinic acid amide or sodium nicotinate are effective in the treatment of pellagra. For the vegetarians we have found buttermilk, and overripe bananas given every two hours or every hour alternately, very useful. Buttermilk is given 6, 8 or 10 ounces every 2 hours, 48 to 80 ounces in 24 hours. Overripe bananas are given 2, 3, or 4 every 2 hours. Most patients can take 12 to 24 or more bananas easily in 24 hours if given when the skin is quite black. The senior author has experience with bananas for the last twelve years and has never found them to fail in diarrhoea of sprue, pellagra, or nutritional anaemia in the adults or in children. The diarrhoea is checked and the weight begins to increase after a few days. Milk is added as soon as tolerated, and later on other articles of diet, the patient should be getting 3000 to 3500 calories per day. 300 mgm of nicotinic acid per day by mouth are enough in most cases. Two tablets, each of 50 mgm are given 3 times a day. In bad cases 500 mgm per day may be required and Spies has suggested that it may be given in ten doses of 50 mgm each, at hourly intervals. This method of giving nicotinic acid is more effective because the controlling factor in the treatment is the concentration of compounds of nicotinic acid in the blood and tissues. All our patients had liver injections and full doses of iron by mouth.

Goldberger has suggested the possibility of pellagra sine pellagra in patients who had gastro-intestinal symptoms, glossitis and nervous symptoms, but did not develop skin lesions. Fitzgerald has described an outbreak of severe glossitis with

ulceration at the angles of the mouth, salivation, gastrointestinal symptoms and diarrhea which occurred in an Assam prison Aykroyd and Krishnan have described stomatitis in children in South India due to deficiency of some factors of Vitamin B₂ complex. They did not observe any involvement of the central nervous system and nothing suggesting pellagrous dermatitis or diarrhea was present in their cases. The disease is curable by fresh or autoclaved yeast, liver and skimmed milk. They suggested that the condition may be a manifestation of flavine deficiency. This raises the question of the etiology of glossitis which is such a common symptom in persons suffering from nutritional anaemia, pernicious anaemia and sprue. We have seen severe stomatitis and angular cheilosis develop in children and adults in cases of enteric fever. The tongue cleared out after nicotinic acid but the angular stomatitis only disappeared after injections of riboflavin. In glossitis of any origin we have regularly used nicotinic acid for the last four years with very gratifying results.

It is difficult to discuss the etiology of pellagra in these patients in Bombay. Was their diet deficient in P-P factor or was there a defective absorption? In answering this we are in full agreement with the leader writer in the British Medical Journal, November 22, 1941, who says

"Pellagra presents a medical conundrum which may be taken as an analogue of sprue. As is well known, this is a comparatively common disease of tropical and subtropical countries in rural inhabitants subsisting upon an unbalanced dietary deficient in protein, and it is curable by nicotinic acid. In many features pellagra resembles sprue in the association of glossitis and stomatitis, frequent diarrhoea with occasional steatorrhoea, achlorhydria, and sometimes anaemia of the pernicious type. In its geographical distribution pellagra frequently overlaps sprue. Thus Wood showed that pellagra and sprue are closely associated in the southern States of the U S A, and other observers (Manning) have described a mixture of sprue and pellagra in the West Indies as *Psilosis pigmentosa*, while it is certain now that the pellagra syndrome (with characteristic dermatitis) may be grafted upon sprue as also upon coeliac disease and idiopathic steatorrhoea. In pellagra mouth symptoms may long precede the fully developed disease, and these cases have been termed 'larval pellagra' or 'prepellagra'. In a substantial number the fully developed picture of pellagra

may never ensue, though equally amenable to nicotinic acid therapy. Manson-Bahr claims that the same localized manifestations may appear in sprue and should therefore be known as 'presprue' or 'larval sprue'. In a fairly high proportion the pellagious manifestations are secondary to destruction of the absorptive surface of ileum and large intestine by tuberculosis, chronic amoebic or bacillary dysentery, or even surgical intervention. Hence the incidence of pellagra appears to depend not so much upon the lack of nicotinic acid in the diet as on the failure of the intestinal mucosa to absorb it."

PELLAGRA

An analysis of 15 cases

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Pellagra is a chronic non-contagious system disorder, a bodily reaction to the lack of some nutritional essential, characterized clinically by cutaneous, gastro-intestinal and nervous manifestations. The condition is endemic in Italy, Spain, Egypt and other parts of the world. In India it occurs sporadically. Fifteen cases were treated in the K E M Hospital as in-patients during the last five years, and we give below a short summary of the case reports and an analysis of their symptoms. Unfortunately the notes are very incomplete, and we give them for what they are worth.

Case 1 A Hindu lady aged 20, vegetarian, complained of pain in the abdomen, swelling of feet, inability to walk and dark brown pigmentation on the hands and feet. She did not co-operate in obtaining the history, had a poor memory and a staling look and failed to recognise the place or the persons. The nervous system examination showed signs of spastic paraplegia, without involvement of the posterior columns. The skin showed dark brown pigmentation with scaly rough skin on the back of the hands and feet. The blood showed a hypochromic anaemia. The Kahn test was negative. Gastric analysis was not done. She was given full vegetarian diet with iron and pepsin mixture, and injections of sodium thiosulphate and campolon. She left hospital against medical advice after a stay of fourteen days.

Case 2 A Hindu female of 30, vegetarian, admitted for pigmentation and scaling of the skin of hands and feet, and diarrhoea of six months' duration. The skin of the hands and feet was dark brown rough and scaly. Appetite was poor, the tongue pale white, the liver and spleen normal. The bowels were loose with four to five watery stools per day. The blood showed red blood cells 4.5 millions per cu mm, Hb 69 per cent, C I 0.7. Gastric analysis showed complete achlorhydria. The stools did not show any abnormality and the blood Kahn reaction was negative. She was given a full vegetable diet with green vegetables, tomatoes,

oranges and marmite. She was put on bitter stomachic mixture, abidol, extralin and injections of sodium thiosulphate. She regained her appetite, strength and weight, the skin lesions and anaemia gradually improved and was discharged from hospital after 35 days.

Case 3 CR a Hindu male of 29 years was admitted in the hospital for the following complaints: (1) inability to walk—2 months, (2) tingling and numbness—2 years, (3) brownish pigmentation on face and limbs—2 months. He did not take alcohol and did not give any history of previous illness. There were dark brown patches on the skin of forehead, malar region and hands. C N system showed signs of spastic paraplegia. No sensory disturbances were recorded. Gastric analysis showed achlorhydria, and the blood showed RBC 4.18 million per cmm. He was put on iodide, pepsin and iron mixture, and injections of campolon 5 c.c. and sodium thiosulphate. After a brief stay of 15 days in the hospital he left against medical advice. The pigmentation diminished to a certain extent but there was no improvement in the nervous manifestations.

Case 4 VD a Hindu male aged 36, carpenter by occupation was brought to the hospital for swelling of the feet, pigmentation on the dorsum of the hands, forearms, feet and lower one third of the legs. He was a non-vegetarian and did not take alcohol. There was burning sensation and marked itching. Cardio-vascular system did not show any abnormality. Blood pressure was only 94 mm of Hg Systolic and 54 mm of Hg diastolic. The blood showed red blood cells 3.12 million per cmm, Hb 60 per cent, CI 0.9, and the gastric analysis showed achlorhydria, the blood Kahn reaction was negative. He was put on marmite, pepsin and iron mixture and was given injections of sodium thiosulphate. The skin lesions improved in about three weeks after admission and had completely disappeared in 45 days.

Case 5 VV a Hindu male of 27, was admitted for (1) brownish pigmentation on the malar region of the face, wrists, round the ankles and feet, (2) severe itching and rough skin, (3) weakness and loss of appetite. The blood showed moderate anaemia and Kahn reaction was negative. He was given full diet, ferri and pepsin mixture with marmite and injections of sodium thiosulphate. The skin lesions improved and the ichthyotic skin was replaced by smooth skin, when he left hospital after 34 days' stay.

Case 6 SG a Hindu lady of 55, was brought to the hospital for frequency of stools for 8 months, loss of appetite and general weakness, and roughening and pigmentation of the skin of the face, legs, feet and hands. Her tongue was pale and smooth and showed dark brown pigmentation at the margins. Her red blood cells were 3.2 million per cmm and Hb 75 per cent, CI 1.18. Gastric analysis showed achlorhydria. She was treated with iron, marmite and liver extract and showed a remarkable improvement. She was dis-

charged after 27 days, when the pigmentation of the skin had entirely disappeared. The general condition had improved and the diarrhoea was controlled.

Case 7 K B a Hindu female and a non-vegetarian, was admitted for brownish pigmentation of the skin on the dorsum of hands, loss of appetite, and general debility. She was treated with iron and cod liver oil mixture and was given 35 injections of 1 c.c. Vibex and 10 c.c. sodium thiosulphate. After a stay of 37 days in the hospital she was discharged, relieved of her symptoms. Unfortunately the detail investigations of the case are not available, but she had regained her appetite and the pigmentation had entirely disappeared.

Case 8 L C a Hindu lady aged 50, was admitted for inability to walk—6 months, scaly ichthyotic condition of the skin on dorsum of hands and feet with brownish pigmentation, and sharply limited from the normal skin by a raised irregular border—2 months, red and glossy tongue. She had signs of spastic paraplegia without any sensory disturbances. The blood showed red blood cells 4.29 million c/mm Hb 70 per cent, C.I. 0.8. Gastric analysis showed achlorhydria, and Kahn reaction was negative. She was treated with pepsin and iron mixture and marmite, liver was given by mouth as well as intramuscularly. She was discharged after a hospital stay of 57 days during which time her general condition had improved. The pigmentation of the skin had cleared up and the skin had become smooth. There was no change in the neurological complaints.

Case 9 D B, a Hindu male, aged 25, was admitted for pigmentation of the skin on the dorsum of the hands and feet—one month, four to six watery stools per day—4 months. The blood showed red blood cells 3.4 million per c/mm Hb 53 per cent C.I. 0.8. The Kahn reaction was negative and gastric analysis showed achlorhydria. Stools and urine N.A.D. He was given pepsin and iron mixture, and was given cod liver oil by mouth and 5 injections of 10 c.c. sodium thiosulphate. He left hospital against medical advice after a stay of 23 days. The frequency of stools was controlled and general weakness disappeared. The pigmentation of the skin persisted.

Case 10 A M a Muslim female aged 25, was admitted for dark brown thickened patches of skin on the forehead, around the neck, on the extensor aspect of the forearms and legs. The lesions were itchy. Loss of appetite, raw red tongue, general weakness. The blood showed red blood cells 3.72 million per c/mm Hb 61 per cent C.I. 0.8. Gastric analysis showed achlorhydria, urine no haematoporphyrin. Stool N.A.D. She was treated with pepsin and iron mixture and was given Vibex liquid by mouth and by injections, and was given four injections of 10 c.c. sodium thiosulphate. There was no improvement.

and consequently she was put on 300 mgms of nicotinic acid per day. Her condition responded remarkably well to this treatment and the scaling ceased. The rough skin was replaced by smooth normal skin, the appetite improved, and her general condition was much better when she was discharged after a stay of 42 days.

Case 11 MB a Hindu female aged 30, was admitted for (1) Rough and brownish pigmentation of the skin of both superior extremities and the dorsum of the feet with fine brownish desquamation. The lesions were clearly demarcated from the normal skin by an irregular line of pigmentation—6 years. (2) Red, raw tongue with superficial ulcers on the border of the tongue and the buccal mucosa. (3) Repeated attacks of frequency of loose watery-stools. The blood showed red blood cells 3.76 million per cmm, Hb 50 per cent, C.I. 0.66. Gastric analysis showed achlorhydria and Kahn reaction was negative. Stool—N.A.D. She was treated with iron mixture and 300 mgm of nicotinic acid per day for 15 days. The diarrhea was controlled, the stomatitis disappeared and her skin condition improved considerably. The scaling had stopped and the pigmentation had partially disappeared and the skin had become smooth.

Case 12 SR a Hindu boy aged 14, was admitted for (1) Dry ichthyotic condition of the skin on the forearms, the folds of the elbows and knees, the axillae and the buttocks with dark brown pigmentation. (2) Stomatitis. (3) Loss of weight and generalized weakness. The blood showed red blood cells 2.88 million, Hb 27.8 per cent, C.I. 0.5. Gastric analysis showed achlorhydria, Stool—ova of *ankylostoma duodenale* seen. Urine—No haematoporphyrin. He was treated with iron and pepsin mixture and tablets of 50 mgm nicotinic acid. Within a month his appetite had improved remarkably, he had increased 12 lbs in weight, the dryness and roughening of the skin had disappeared, the pigment had a lighter hue and his red blood cells had gone up to 3.7 million, and Hb to 50 per cent. He was discharged after a hospital stay of 54 days completely cured.

Case 13 RR a Hindu male aged 40, was admitted for (1) Scaling, thickening and pigmentation of the skin over the hands, legs and feet for 5 months. (2) Raw and red tongue with brownish pigmentation at the borders. (3) Pigmentation of the mucosa over the palate. (4) Spleen enlarged 3" below the costal arch. The blood showed 3.2 million red blood cells, Hb 69 per cent, C.I. 1.07. Gastric analysis showed achlorhydria, Urine—no haematoporphyrin. He was treated with pepsin and iron mixture and nicotinic acid tablets of 50 mgm each, by mouth. The skin lesions cleared away very rapidly. He was also given 14 injections of 10 cc sodium thiosulphate. After the skin lesions were cured treatment with iron and pepsin was continued and he improved remarkably well and gained 18 lbs in weight during his stay of 3 months in the hospital.

Case 14 B D a Hindu male aged 20, was admitted for (1) Breathlessness on exertion—1 month (2) Oedema of feet, pitting on pressure, for 10 days (3) Dry exfoliative pigmented eruption on the dorsum of the hands (4) Engorgement of veins in the neck, enlarged tender liver, enlarged heart and tachycardia (5) Signs of chronic bronchitis in the lungs The blood showed red blood cells 1 24 million per c mm Hb 25 per cent C I 1 Gastric analysis showed Hypochlorhydria, Kahn reaction was negative, blood chemistry was normal, Urine—Haematoporphyrin positive Stool—NAD He was first treated on the usual lines for congestive cardiac failure and when that condition was improved he was given nicotinic acid tablets of 50 mgm each His general condition improved, and the skin lesions cleared away when he was discharged after a stay of 2 months The urine showed no haematoporphyrin and his red blood cells had increased to 4 6 million per c mm and Hb to 80 per cent

Case 15 S A a Muslim male, aged 30, a coolie, was admitted for (1) Roughening and brownish pigmentation of the skin on the dorsum of the hands and feet—6 months (2) Ulcerations of the buccal mucosa, (3) Pigmentation of the tongue, (4) Constipation (5) General weakness The blood showed red blood cells 1 92 million per c mm, Hb 30 per cent, C I 0 8 Gastric analysis showed achlorhydria, Stool—NAD Urine showed no haematoporphyrin, and the Kahn reaction was negative He was treated with acid hydrochloric dilute and iron mixture and was given 200 U S P units of liver extract intramuscularly and nicotinic acid tablets of 50 mgm each The pigmentation cleared off wonderfully and the skin became smooth His red blood cell count came to 4 2 million c mm and Hb 75 per cent after a stay of 35 days in the hospital His appetite improved remarkably well and he could easily take a diet of 4,000 cal per day His weight increased from 89 lbs to 107 lbs when he left the hospital The stomatitis showed only a partial improvement and when he went away he had a few ulcers on the buccal mucosa

An analysis of the foregoing 15 cases shows the following facts

Age Incidence The disease, though occurring at any age, is most common between 21 and 30 years The age incidence was as follows —

10—20	2
21—30	9
31—40	2
41—50	1
51—60	1

Sex The disease occurs in both sexes Males 9, and Females 6

Diet Of the fifteen cases only four were vegetarians and eleven were taking a mixed diet

Occupation It is interesting to note that of the 9 males 6 were unemployed, 1 was a coolie, 1 a carpenter and 1 a motor driver

Alcoholism and Syphilis are often blamed as predisposing causes but in our series we did not get a single case of this type

Of the variously described symptoms the most common is the dermatitis. It was present in all the 15 cases and varied from slight pigmentation and roughening of the skin to dark brown pigmentation, ichthyosis, scaling and the presence of hyperkeratotic borders. In no case did we find the severe condition in which bleb formation or ulceration is described. The dermatitis was always symmetrical, bilateral and on the exposed parts of the body

Gastro Intestinal Disturbances Of the 15 cases reviewed 7 had anorexia, 6 had stomatitis and 5 glossitis. Only 4 cases out of the 15 had diarrhoea and 3 had definite constipation

Nervous Symptoms Only one case out of the 15 under review had mental disturbances while 4 had spastic paraplegia without involvement of the posterior columns. We may mention that in most cases there is no record of a detailed clinical examination of the nervous system

Anaemia All the fifteen cases had anaemia but of these 13 had microcytic hypochromic anaemia while 2 had hyperchromic anaemia (6 and 14)

Achlorhydria Of the 15 cases reviewed only 12 were investigated from this point of view and of those eleven cases showed achlorhydria and one showed hypochlorhydria

Haematoporphyrimuria 5 cases were investigated with this end in view and only one case showed definite haematoporphyrimuria (No 14)

Associated Diseases Two cases had intestinal parasites—*ankylostoma duodenale* and *ascaris lumbricoides*—while one case had congestive cardiac failure

Response to Treatment 6 cases were treated with varying amounts of nicotinic acid ranging from 100 mgm per day for

12 days to 300 mgm per day for 29 days according to individual requirements and they all responded very well. The rest were treated without nicotinic acid, but were getting yeast, marmite or crude liver extract. Of these 9 cases were cured, 4 found partial relief, while 2 were not benefitted at all due to an insufficient stay in the hospital.

The attempt at analysis of the foregoing cases reveals some interesting features, and though it is felt that the evidence available is not all that one would like to have and the data is incomplete, it shows that pellagra is not so rare as one would think and many early cases are likely to be missed unless specially looked for. The cases of severe anaemia which show pigmentation and stomatitis with diarrhoea are difficult to differentiate from pellagra. From the foregoing analysis it is clear that certain data must be present to permit a diagnosis of pellagra. The most important evidences are

A bilateral, symmetrical pigmentation of the skin of the exposed parts, e.g., hands, feet, forehead and face. This pigmentation must necessarily be accompanied by at least a roughening of the skin, if not by ichthyosis and scaling. We do not know of any "pellagra sine pellagra (rough skin)".

The other important thing is the presence of anaemia. More often it is a microcytic hypochromic anaemia but may be macrocytic hyperchromic. Gastro-intestinal symptoms—*anorexia*, stomatitis, diarrhoea,—are always present. Nervous and psychotic symptoms are also present.

The third important finding, though not absolutely essential, is the absence or diminution of free hydrochloric acid in the stomach.

The fact that pellagra, like anaemia, is inspite of a balanced diet commonly found in people who have malignancy of the stomach or have been operated upon for duodenal ulcer, suggests that the mucosa of the stomach has an important role in the assimilation of P P F.

The above considerations show that not much of laboratory aid is required in the diagnosis of pellagra and the diagnosis is within easy reach of the general practitioners even in the most rural.

As to the treatment of pellagra we would mention the part that vitamin B has played in revolutionising our concept of Vitamins and their therapeutic value. The history of Vitamin B complex is very much the history of vitamins. It was as early as 1925 that Goldberger, Tanner and Joseph isolated their P-P factor from Vitamin B₂ complex which was later on shown to consist of riboflavin P-P factor, filitrate factor and several undetermined factors. At first it was thought that whole vitamin B₂ complex was necessary for the treatment and prevention of pellagra, but Rhodes and Miller in 1935 showed conclusively that black tongue in dogs, which is analogous to human pellagra, could not be produced on a riboflavin free diet nor could it be treated with a flavin supplement. Yet some still think that deficiency of more than one factor is responsible for producing pellagra and they describe the cases which had other manifestations of pellagra but no dermatitis (Pellagra sine pellagra) and which responded to yeast treatment. They claim that dermatitis is due to the deleterious effect of sunlight on the skin. This view is a very old one and dates back to Frapolli (1771) but in 1937 Smith and Ruffin succeeded in producing the skin lesions once again in 13 out of 35 pellagrins treated and cured, and this led them to think that pellagral dermatitis was due to the trauma inflicted by sunlight. Sydenstricker and Thomas suggest that the dermatitis is due to photosensitization of the skin by haematoporphyrin excess in blood. From the evidence at present available, it can only be said that pellagrins are more sensitive to sunlight than non-pellagrins.

The exact nature of nicotinic acid, which has found such an eminent place in the treatment of pellagra, is not known. It may be P-P factor itself or a provitamin or one of the two or more substances needed for prevention of pellagra or it may be the substance that is conjugated with other substances in the body into a complex essential material necessary for prevention of pellagra. At present little is known about its physiologic action, but its importance in treatment cannot be doubted now.

For an ordinary case of early pellagra Goldberger, Sebrall and Spies emphasise that all that is required is a diet of 4,000 cals with adequate P-P factor. Such a diet should mostly be made up of milk, fresh leafy vegetables, legumes and lean

meat, liver, haddock and salmon For advanced cases of pellagra the following is the treatment advocated —

A diet of 3 to 4 thousand calories consisting of substances rich in P-P factor

Frequent feeding

Nicotinic acid varying from 60 mgm per day for 12 days to 500 mgm per day according to individual requirements

- Symptomatic treatment—here it may be mentioned that if cheilosis resists nicotinic acid treatment it may respond to riboflavin

Yeast and liver extract

Prevent recurrence by a permanent change in diet or a supply of yeast powder or nicotinic acid

Our thanks are due to the Dean and the Hon Physicians of the K E M Hospital, for permitting us to make use of their case records and to Dr N D Patel, for suggesting and guidance in this review

CLINICAL EXAMINATION OF PATIENTS FOR NUTRITIONAL DEFICIENCIES

Nutritional deficiencies are extremely common among the poorer class of patients, who live on poor and monotonous diets. They are also common among the school children, the inmates of orphanages, boarding schools, asylums and prisons. Among the well-to-do also one meets them frequently as a result of some food-fad, or some disease which prevents the absorption of the dietetic essentials or as a result of cooking which destroys them. In diseases such as enteric fever, peptic ulcer, ulcerative colitis, or spire a variety of manifestations of dietetic deficiency may appear as a result of a special diet or a lack of absorption. Alcoholics, diabetics and women during pregnancy or lactation also show a variety of deficiency manifestations. To detect these it is desirable to have a routine method of examination in order not to miss the minor manifestations.

Eddy and Mills point out that vitamin deficiency may exist at two levels. The first is that of disturbed physiology accompanying the early stages of interference with the chemical process of the cells. Physical signs which depend on structural alteration are not present. When this deficiency becomes more advanced the second level, that of anatomical change, is reached and the classic signs of deficiency disease appear. The recognition of frank rickets, scurvy, pellagra or beriberi, wet or dry, is not difficult. What is difficult is to detect subclinical deficiencies.

Standards of the State of Nutrition

Aykroyd suggests 3 different methods by which the state of nutrition in individuals may be assessed.

- (1) Comparison of certain measurements with a chosen standard, e.g., Height and Weight
- (2) The correlations of certain measurements of the arms, chest, and across the hips, the mean A C H index, or,
- (3) The measurement of the circumference of a limb, such as the arm over the biceps, from time to

time This mean length of circumference of the arm is correlated with the height and weight of the growing child In using the height and weight one must remember the racial and familial variations Again, a child fed on a diet over-rich in carbohydrates may be over weight, and yet in a state of malnutrition

From the measurement of the height and weight, we get the following groups —

10% or more below average weight for height=
malnutrition

Under average weight but less than 10 per cent =
borderline

Average weight, or 20 per cent above=*normal*

20 per cent or more above average = *overweight*

The regularity in gain of height and of weight are of more value in infancy and possibly throughout childhood, though seasonal variations in growth and also variations of rate at different ages—the rhythm of growth or what Harris has described as ‘stretching up’ and ‘filling out’ periods must be borne in mind

Clinical Methods

On a general clinical examination, an experienced physician gets an impression of the nutritional state of the person which is quite reliable Unfortunately, different observers rarely employ the same criteria, and if the personal findings are to be of any use to others, it is necessary that the criteria, by which clinical assessments are made by the physician should be defined

A critical survey of (1) colour of the skin, lips, gums and palpebral conjunctiva, (2) amount of subcutaneous fat, (3) texture of skin, elasticity, (4) texture and tone or activity of muscles, (5) structure of bones and skeleton as a whole, (6) alertness or aliveness, and (7) fatiguability, gives an experienced observer reliable data about the nutritional state of the person After such a clinical assessment the state of nutrition is noted as excellent, good fair requiring supervision, or seriously

impaired requiring medical treatment. In making such a clinical assessment the following points may be noted --

(1) **Skin.** As a result of dietary deficiencies a number of pathological changes occur in the skin and in the subcutaneous tissues. These are

- (a) **Phrynoderma** or follicular hyperkeratosis
- (b) **Pellagra-like eruptions**
- (c) **Haemorrhages**
- (d) **Oedema**

(a) **Phrynoderma** results from changes in the sweat and sebaceous glands. It is very common among children of the poorer classes. It commonly occurs on the extensor surfaces of the arms just above the elbow, or there may be a generalized affection. The superficial epidermis and the sebaceous and sweat glands are affected. In some cases there is dryness and wide-spread scaliness of the skin, and slight enlargement of the sebaceous glands, especially those on the extensor surfaces of the limbs, or there may be a marked non-inflammatory enlargement of the sebaceous glands and the formation of horny matter plugging the sebaceous follicles. This papulo-follicular dermatosis known as toadskin is said to result from a deficiency of vitamin A.

(b) **Pellagra-like eruptions.** *Dark irregular patches* of parchment texture are seen on the cheeks, back of the hands, feet, and other exposed surfaces. There is a tendency to peel and expose small areas of a lighter colour, this gives the eruption a blotchy appearance. There may be a bleb formation and marked ulceration. Scrotal and perineal dermatitis with eczema and oedema of the subcutaneous tissue making the scrotum larger than normal may be present and in females there may be a similar condition of the vulva.

(c) **Haemorrhages** occur as petechiae in the superficial areas of the skin or larger haemorrhages in the subcutaneous tissues causing indurated swellings with pigmentation, or a subperiosteal haemorrhage with intense pain may occur in the presence of vitamin C deficiency.

(d) **Oedema** due to improper diet starts around the ankles and later may be generalized. It is common in malnourished

children and extremely frequent among adults of the poorer classes whose diets have a shortage of protein

(2) **Hair.** In children the hair is dry and staring sometimes accompanied by scurviness. In adults there may be dryness and premature graying

(3) **The Mouth Stomatitis** Perhaps this is the most frequent sign of dietetic deficiency met with among all classes of people in India. There are red patches of superficial erosion of the mucous membrane of the tongue which make a marked contrast to the unaffected parts of the tongue which are covered with normal fur. The papillae are disappearing and the mucous membrane is smooth as if rubbed with sand paper. There may be a general atrophy of the tongue. In severe cases the ulcers may extend to the cheeks the soft palate and the pharynx.

(4) **Lips** may be affected especially at the angles of the mouth, and this cheilosis or angular stomatitis has been used by some investigators as a sure sign of nutritional defect in rapid nutritional surveys

(5) **Oesophagitis** Pain on swallowing is a well known symptom in certain cases of anaemia. When associated with achlorhydria and anaemia the condition is described as Plummer-Vinson syndrome. It is very common in women with anaemia, or during pregnancy or lactation and should not be dismissed as hysterical globus.

(6) **Gums** may show hypertrophy—'Scurvy buds'—and a tendency to spontaneous haemorrhages or haemorrhages on slightest trauma such as pressure or brushing. Deficiency of vitamin C is the cause. Bleeding may lead to secondary infection with enlarged glands in the neck.

(7) **Teeth** Dental decay is very prevalent in all classes of people in India, and at all ages. Many children show black decayed stumps of milk teeth. Malocclusion and irregularities of the teeth resulting from a stunting of the forepart of the jaws due to malnutrition in infancy, are common in adults. Deficiency of calcium and phosphorus in diets or a deficiency of vitamin D may account for the dental decay.

(8) **Eyes** Night blindness is an early symptom of vitamin A deficiency. This is due to the disappearance of the visual purple in the retina, which cannot regenerate in the absence

vitamin A Bitot's spots are yellowish irregular patches on the conjunctiva, and often seen in poorer classes of school children

Xerophthalmia — Keratomalacia — Keratitis — These eye-troubles occur at any age but are most frequent in infants after the time of weaning when the child is fed with a diet with very little vitamin A. Deficiency due to faulty feeding is the direct cause of preventable blindness in children. Breast-fed infants do not develop eye troubles

(9) **Bones** Deformities of limbs and epiphyseal enlargements. Skull bossing. Ricketsy rosary

(10) **Muscles** Tenderness, lack of tone, weakness and paresis may occur in cases of vitamin B deficiency. Muscular dystrophies

(11) **Nerves** Changes in nerves and spinal cord of animals which have been fed on diets deficient in vitamin B₁, A, B₂ or C are noted. Neuritis is defective in vitamin B especially in chronic alcoholics, diabetics and women during pregnancy. Pain, numbness, tingling sensations in the hands and feet and vague pains all over the body—"rheumatism"—are early symptoms. Deep muscular tenderness on pressure and variations in tendon reflexes with sensory changes such as inco-ordination, and muscular weakness and paresis are physical signs

(12) **The Blood** may show a microcytic hypochromic or macrocytic hyperchromic anaemia as a result of malnutrition

(13) **Infections** Catarrhal infection are very common in persons with vitamin A deficiency

(14) **Growth** Diets deficient in protein or in vitamins and in minerals result in stunting of growth in experimental animals and most probably it is the same in growing children

The Laboratory Diagnosis of Nutritional Defects

Unfortunately the laboratory tests for the measurement of nutritional deficiencies are not simple and easy to carry out. Except the simple procedures, such as the estimation of haemoglobin and enumeration of red blood cells, the estimation of blood calcium and the X-ray examination of the bones, others are not available for clinical use. The estimation of visual

recovery or the dark adaptation test for vitamin A deficiency, Harris's method of estimating quantitatively the urinary excretion of vitamin B₁, or the estimation of vitamin B₁ in the blood by the mould-growth, or the estimate of vitamin C reserves are not yet within the reach of clinical practice

Table modified from Eddy and Mills

Vitamin	Symptoms	Signs	Daily Therapeutic Doses
Vit A	Night blindness	Dry scaly skin Icteric or Hyperkeratosis—Ford Skin Bitot's spots Xerophthalmia keratomalacia Dry string hair	50 000 to 100 000 U.S.P. units
Thiamine or Aneurine B ₁	Anorexia Cardiac failure Pains all over Paresthesia	Deep muscle tenderness Tendon reflexes altered Loss of vibration sense Tachycardia Oedema	20-30 mgm
Riboflavin B	"	" Cheilosis Seborrheic dermatitis Keratitis Glossitis	5 mgm
Nicotinic acid I.P.I.	Painful mouth and tongue Diarrhoea Dermatitis Stupor Psychosis	Inflamed denuded tongue Dermatitis—symmetrical limbs face scrotum vulva perineum C.N.S. signs	250-500 mgm
B ₆ Pyridoxine Bitanti dermatitis	Weakness Insomnia Nervousness	" Angular stomatitis or cheilosis	50 mgm
Ascorbic acid	Bleeding Pain	Petechiae Spontaneous haemorrhages Gums spongy	500-1000 mgm
D	Weakness Rickets	Cessation of bone growth Deformities Disturbed Ca-P metabolism Osteoporosis Dental decay	1200-60 000 U.S.P. units
E	Stillbirth abortion	Muscular dystrophy " Motor Neurone disease "	"
K	Bleeding	Petechial and Spont. haemorrh	1 mgm

Critical Notes and Abstracts

NON-SPECIFIC ILEOCOLITIS (Crohn's Disease)

Non-specific Ileocolitis was described by Crohn in 1932. Later on he described Ileojejunitis which is less frequent and affects the bowels higher up. Mayo and Judd (JAMA, September 6, 1941, p. 836) report a hundred cases of Non-specific Ileocolitis where surgical resection was performed. Of the hundred patients, 54 were men and 46 women. The average age was 32.5 years. The average duration of symptoms was 2.6 years, with a range of one week to 18 years. The outstanding symptom was *diarrhoea*. Some patients had noticed *a lump on the right side*. The appendix had been removed recently in certain cases. Some had persistent discharge of serum, pus or fecal material, from an appendectomy wound, which prompted them to request surgical intervention. Marked anaemia was not a feature of this group of patients. Prolonged diarrhoea with attendant chronic dehydration appeared to have produced hemoconcentration, giving relatively high blood counts out of proportion to the obvious condition of the patient. In most cases the x-ray reports were highly accurate and clearly established the diagnosis and defined the extent of the disease process. Two or three examinations with barium sulphate meal were necessary. The treatment is surgical resection, either one, two or multiple stage. The follow up showed that the longer the patient survived after resection whether it had been performed in one stage or more stages the better subjective or objective results appeared to be. Thorek suggests that ileitis may appear as a universal colitis affecting all the colon and rectum or it may start at one point and extend in either direction. He considers deficiency diseases and faulty fat metabolism in the differential diagnosis. The x-ray images are typical narrow areas alternating with skip area dilatations. The "string sign" is most usually proximal to the ileocecal valve. Medical treatment is rarely successful. Spontaneous cure is rather frequent, hence surgical intervention in the acute stages is contraindicated. There is no specific treatment. Chemotherapy and x-ray therapy are disappointing, surgical resection of the affected bowel is proper procedure. Crohn suggests that ileum must be resected because if it is not transected the process is likely to spread in an oral direction and the disease extend itself. In his opinion one stage operation was best, and if the patient's condition is improved, as shown by gain in weight, and increase in haemoglobin, there is no point in performing the unnecessary two stage operation. The second stage procedure is indicated if fistula persists, if the temperature is elevated, if the haemoglobin falls and if there is a continuous loss in weight.

NON-SPECIFIC ULCERATION OF COLON

Barlow has described a new syndrome of chronic non-specific Ulceration of Colon, (*Brit J Surg*, April 1941, p 575) which is difficult to diagnose before perforation. When the ulcer is in the caecum or ascending colon the clinical picture may suggest appendicitis, the ulcer may be in the sigmoid colon or even in the rectum. Clinically the condition is characterized by chronic abdominal pain which is less severe than that of gastric or duodenal ulceration. The pain is vague and may suggest malignancy. There are acute exacerbations of the inflammatory process which ends in perforation. The diagnosis is not possible prior to perforation and without laprotomy Barlow suggests that barium-air contrast radiography might help in the pre-operative diagnosis. Pathologically the ulcer resembles peptic ulcer except that it is funnel shaped, the edge is hard and there is active inflammation at the base of the funnel where perforation occurs. The treatment is resection and lateral anastomosis. There is no spontaneous recovery nor any specific treatment. Without operation all cases terminate fatally.

INCIDENCE OF NEUROPATHY IN PELLAGRA

Effect of Co-carboxylase on its Neurologic Signs. F.H. Lewy (Univ of Pennsylvania), T. D. Spies and C. D. Aring (Univ of Cincinnati) studied 50 pellagrins, three fourth of whom were mild or moderately severe cases. The nerve trunks most frequently tender to pressure were the radial, ulnar, occipital, supra- and infra-orbital. Hypoalgesia and hyperaesthesia were usually of the glove and stocking type. An association between decrease of pupillary reflex and abnormal electric irritability of the peripheral nerves suggests that the former is due to the involvement of the motor

TABLE—Incidence of Nervous Signs

Romberg sign	8
Tremor	12
Pyramidal sign	12
Deviation of tongue	18
Nystagmus	20
Extrapyramidal signs	20
Loss of power in arms or legs	22
Decrease of corneal reflexes	23
Ataxia	26
Decrease of tendon reflexes	36
Decrease of pupillary reflexes	38
Decrease of touch sensation	44
Decrease of pain sensation	53
Abnormal electric irritability	71
Tenderness of nerve trunks	74

side of the aic, the oculomotor nerve. An association between decreased corneal sensitivity and decreased pain sensitivity in the extremities is interesting because the corneal nerve endings are essentially of the pain type.

Intravenous administration of 50 mg or more of synthetic cocarboxylase to nine pellagrins resulted in quantitative improvement in electric irritability of a number of muscles in pupillary and corneal reflexes and in sensitivity to touch and pinprick. These reflexes became normal in one to four hours after injection and improvement was maintained for one to five days. There was a tendency to regression with return to the condition preceding treatment. Tenderness of the nerve trunks improved in four of six cases in which it was present. Retention of cocarboxylase was associated with improvement, inability to retain it (excreted in urine), with failure to improve. Return of blood chemistry (bisulfite-binding substances, including pyruvates and arteriovenous oxygen difference) to normal paralleled clinical, neurologic and psychoneurotic improvement. Administration of synthetic riboflavin was not followed by change of neurologic signs. The clinical effect of cocarboxylase was identical with that of thiamine.

These observations confirm the authors' premise that neuropathy which is common among pellagrins is caused by a deficiency of Vitamin B₁.

RUPTURED INTERVERTEBRAL DISKS

In 1929 Walter E. Dandy of Baltimore reported two cases of ruptured intervertebral disk of traumatic origin. Since that time protruded intervertebral disks in the lower lumbar region are recognized as a leading cause of chronic intractable sciatic pain. The clinical syndrome is typical and the condition appears to be most frequent. In 1934 Mixter localized the lesion before there was a total block in the spinal canal by injecting 5 cc of Iodized oil into the spinal canal. In 1937 Reichert substituted air for iodized oil as a contrast medium and reported many cases with excellent diagnostic results. In 1939 Semmes diagnosed 16 cases without any contrast medium whatever, solely by history and neurological examinations. Since then many observers have diagnosed the condition on clinical examination alone. 96 per cent of all the lesions are found at the fourth and fifth lumbar disks fairly evenly divided between these two locations. Dandy (*JAMA* September 6, 1941, p. 821) makes a plea for elimination for all forms of contrast mediums for localization of intervertebral disks and presents observations on the concealed type of ruptured intervertebral disks that cannot be disclosed by intraspinal injections. He considers intraspinal injections unnecessary, misleading, adding to the patient's discomfort and suggests that permanent deposit of iodized oil in the brain and spinal cord is harmful and should be avoided.

The diagnosis is made on the presence of low midline lumbar backache plus pain down the back of one or both legs. The pain is intensified by coughing and sneezing, and it must be recurring and not continuous. When this simple story is obtained there is no other lesion that need be considered. There may or may not be diminution of the ankle reflex or sensory or motor loss in the distribution of the fourth or fifth lumbar or first sacral nerve. The history of trauma which is always the cause may be difficult to elicit and need not be obtained. The injury is usually a minor one such as a heavy lift, a wrench or a sudden movement. The history of recurring pain is essential to the diagnosis and a differential diagnosis from psychogenic backaches which are always present. Dandy considers exacerbation of pain on coughing or sneezing—a pathognomonic sign of a disk or possibly a tumor. It does not occur in psychogenic pain which is constant and not recurring. Iodized oil still remains a necessary test in diagnosing and localizing tumors of the spinal canal. Air shadows are never so good, and the air is soon lost. Dandy considers that if the diagnosis is in question the exploration of the region is preferable to spinal injections of air or iodized oil. The removal of the protruding portion of the disk and the overlying ligamentum flavum offers a quick, complete and permanent relief in a high percentage of cases. Concealed vertebral disks, doubtless explain many of the negative explorations for this lesion. In his series of 37 vertebral disks which he removed in eight months, Dandy had ten (28 per cent) 'concealed disks'. The disk bulges so slightly that it would never be disclosed by iodized oil or air injections into the spinal canal and would be found at the operation only by a careful inspection, beneath the dura. These concealed disks cause root pains because they are adherent to the nerve and not from mechanical pressure on them.

PEMPHIGUS

Commenting on the lack of knowledge of the cause of Pemphigus as the real stumbling block in the path of rational therapy, Gellus and Glass (Arch. of Derm. & Syph. Sept. 1941) give a survey of 170 patients—72 male and 98 female—admitted to the Bellevue Hospital between 1911 and 1941. Between the years 1929 and 1941, 0.8 per cent of all skin cases attending the hospital were suffering from Pemphigus.

The relative mortality for age groups shows the highest male mortality from 40 to 75 years and the highest female mortality between 30 and 34 years, and a diminishing female mortality between 55 and 59 years. This fact may be of value in prognosis.

The earliest lesions appeared most frequently on the trunk in women often on the breasts and mammary folds. Next in order of frequency the mouth, the extremities, the face, the scalp, the eyes, on the neck and in the groins. In a few cases injury or illness appeared to precede the onset. Two cases gave an extremely vague familial

history One stating that a brother-in-law had it six months ago and another, that a cousin suffered from Pemphigus 18 years previous to the patient's own attack

An analysis of common symptoms and signs showed —Itching in 59.3 per cent This symptom the authors point out is held by dermatologists of repute to be against a diagnosis of pemphigus Next comes, loss of weight, burning of the skin, bleeding and soreness of the mouth, weakness, obesity to a decided extent in 10.4 per cent of patients Erythema around the bullae, also a controversial point in diagnosis, was recorded in 4.7 per cent of cases Loss of weight and bleeding and soreness of the mouth generally had a fatal prognosis

Grace writing in *Med Clin North Amer* describes a typical blood picture in pemphigus There is a secondary anaemia with progressively elevated WBC count as the condition worsened, and a rapid fall 48 hours before death There is a shift to the left in the differential ratio as the disease progresses and the increase in eosinophiles noted earlier in the disease, decreases as the end approaches The authors' cases showed a similar blood picture to that recorded by Grace The Pels-Macht phytopharmacologic indexes also supported the diagnosis in 23 out of 27 cases

The results of treatment were not very encouraging Tabulation is under the following headings —

1 Stimulants, included caffeine with sodium benzoate, strychnine, digitalis, and ardenalin hydrochloride

2 Specific remedies included solution of potassium arsenite, neosalvarsan, sodium cacodylate, acetarsone, triparsamide, methythionine chloride, snake venom germanin, sulfanilamide and adrenalin

3 Miscellaneous drugs included potassium iodide, autogenous vaccines, old tuberculin, autohaemotherapy and blood transfusion, quinine, high calorie diet, liquid extract of spleen amniotin and spinal cord vaccine

4 Vitamins included viosterol in oil, high vitamin diet, cod liver oil, liver extract and nicotinic acid

5 Local remedies were boracic ointment and calamine lotion

J A FERNANDEZ

NON-PENETRATING INJURIES OF HEART

The effects, temporary and permanent, of chest-injuries on the heart and circulation had received very little attention from the medical profession until recently, when several papers and one exhaustive monograph have appeared on the subject

In his monograph on "Subacute and Chronic Pericardial and Myocardial Lesions due to non-penetrating Traumatic Injuries" (1938), Warburg (*Brit Med Jour*, (1940) 2 271), has reviewed as many as 202 cases of traumatic cardiac injury. More recently (1940) he has added to the literature a further series of 59 cases. Amongst the various lesions consequent on cardiac trauma, he describes (1) Pericarditis dry, serous or haemorrhagic, a hydro-pneumo-pericardium with a characteristic splash has also been described (2) Auricular Fibrillation, which was noted by Warburg in 20 per cent of his series of cases. Other varieties of cardiac arrhythmia have also been described (3) Partial rupture of ventricular muscle with aneurysmal dilatation. Complete rupture with death may result in such cases after a latent period of two weeks or more (4) Angina pectoris or coronary occlusion are rare sequelae of cardiac trauma.

In this connection, I wish to record two cases of non-penetrating heart injury observed personally. Detailed case-reports not being available, the main features of the cases are presented.

Case 1 A woman aged 40, was seen at St Thomas's Hospital, London, in 1936 by me, as a house-physician. She had a severe degree of aortic incompetence with all its peripheral manifestations. She dated her disease from an injury to the chest one year previous. Her husband in a fit of rage had hurled an alarm clock at her, which had landed over the precordium. Immediately after the impact, she had felt a "snap" in the chest followed by a "loud grating sound" (the diastolic murmur). Previous to the injury to the chest she had been in perfect health. In this case, injury to the chest had apparently resulted in the rupture of an aortic valve cusp with incompetence at the aortic orifice.

Case 2 Recently, a man of 40 was seen in Bombay with a typical history of anginal pains coming on after exertion and relieved by rest or nitrites. The first attack of angina was noted about thirty hours after a chest injury. In his case it was a steel rod falling on his chest while working in a factory. He was positive about the relation of his chest injury. He showed no intention of claiming any compensation either. As he was known to have been in good health previous to the injury it certainly looks as if the trauma was the predisposing factor of angina pectoris in his case.

R J VAKIL

TREATMENT OF ESSENTIAL HYPERTENSION WITH VARIOUS DRUGS

Thus was recently the subject of a laborious investigation at the London Hospital by William Evans and Owen Loughnan (*Brit Heart Jour* (1939) 1 199). They tried the therapeutic effects of thirty-three different medical preparations on 70 cases of Hyperpiesia. The following were some of the preparations submitted to the clinical trial: nitrites, iodides, sedatives, xanthine derivatives, choline substances,

thiocyanates, calcium chloride, benzyl benzoate, vegetable extracts, animal extracts and hormones. Each preparation was prescribed in optimum dosage for fortnightly test-periods and alterations in blood-pressure and change in symptoms recorded.

The authors came to the conclusion that "none of the 33 preparations produced hypotensive effects in patients with hypertensia." Papaverine sulphate and chloral hydrate were the only two drugs producing results slightly better than inert placebo. Symptomatic relief of some sort or other was experienced after only six of the 33 preparations tried: bismuth subnitrate, iodine and iodides, bromides, sodium luminal, theominal and potassium thiocyanate.

R J VAKIL

CONTRAINDICATIONS TO THE USE OF THE ERGOTAMINE TARTRATE

According to Von Storch, (JAMA 111 293, 1938) the use of Ergotamine Tartrate in migrainous headaches is not attended by any serious consequences unless the drug is used indiscriminately. Serious sequelae such as gangrene, reported in the literature, are due in the opinion of the author, to one of the following causes: (1) overdosage of the drug, (2) pre-existing sepsis and (3) obliterative vascular disease including coronary sclerosis. He recommends caution when using this drug in cases of arteriosclerosis, hepatic diseases, kidney disease and Vitamin C deficiency.

R J VAKIL

DISTINGUISHING PHYSIOLOGICAL TACHYCARDIA FROM TACHYCARDIA SECONDARY TO MYOCARDITIS

Waller (Ztschr f Kreislaufforsch 30 481, 1938) has demonstrated a useful electrocardiographic sign for distinguishing physiological tachycardias (such as secondary to exercise) from those resulting from myocardial disease. In the former types, there is no accompanying prolongation of the aunculo-ventricular conduction time as shown by an increase of P-R interval. In myocardial diseases, on the other hand, a prolonged P-R interval is an important and early sign.

R J VAKIL

ELECTRO-CARDIOGRAPHIC ALTERATIONS INDUCED BY ACIDOSIS AND ALKALOSIS

In 1926 Schott demonstrated for the first time the effect of intravenous injections of HCl and of NaCO₃ in dogs, on the T wave of the cardiogram. The T wave was shown to increase in size in acidosis and became smaller in alkalosis. Since that time several observers have commented on the effects of acidosis and alkalosis on the amplitude of T (waves) and on the duration of electrical systole (the Q-T interval) in man. On the basis of a new study, Barker, (Amer Heart Jour 17 169, 1939), and others have recently arrived at the following conclusions: (1) Alkalosis, induced by voluntary overventilation or by

ingestion of sodium bicarbonate, leads to reduction in amplitude of the T wave (2) Acidosis, induced by exercise or by ingestion of Ammonium Chloride, leads to increase in the amplitude of the T wave (3) There is however no direct quantitative relationship between the amplitude of T and the degree of acidosis or alkalosis (4) These workers found no significant change in the duration of the electrical systole with acidosis or alkalosis as described previously by other authors. The authors are at a loss to explain the modus operandi of these electrocardiographic alterations

R J VAKIL

IRRADIATION OF ADRENALS FOR ANGINA

According to Raab and Schonbrunner, (Archiv fur Kreislauff Dresden 4 189 (1939) abstr from JAMA (1939) 113 632) angina induced by exercise, emotion, cold etc is probably due to excessive liberation of adrenalin from the suprarenal glands. Since X-ray irradiation of these glands resists the production of adrenalin, they tried this form of treatment in 38 cases of angina, 28 of these were improved or cured after treatment. Electrocardiographic follow up showed that out of 13 cases with electrocardiograms suggestive of myocardial anoxaemia, 10 were more or less restored to normal after treatment. In the opinion of these authors, their study, clinical and electrocardiographic, leaves no doubt as to the efficacy of this treatment in cases of angina

R J VAKIL

EXTREME GRADES OF CARDIAC ENLARGEMENT

A careful search of the literature by Golden and Brans (Amer Heart Jour (1937) 13 207) for records of hearts weighing 1000 g or over revealed that 38 such cases had been reported in the last century. The largest heart on record weighing about 5 lbs was reported by Sedgwick and again by Wood.

The most frequent causes reported were pericardial adhesions and diseases of the aortic valves. In some instances of extreme cardiac enlargement even thorough investigation failed to reveal any causative factor. Such instances have been labelled "Idiopathic cardiac hypertrophy."

R J VAKIL

EVOLUTION OF PAPAVERINE HYDROCHLORIDE AS A VASODILATING AGENT

Papaverine was first identified as an alkaloid of opium in 1848 by Meier. It was prepared synthetically by Pictet and Gans in 1909. But after much work on this drug has come to the conclusion that papaverine relaxes smooth muscle throughout the body by direct action on muscle fibres. Denk, (Munchen med Wehnschv 81 437 1936) using a preparation closely allied to Papaverine (viz, Eupaverine) in intravenous doses of 0.03 to 0.06 g obtained excellent results in cases of acute embolism of major blood-vessels in the extremities. There was complete restoration of the circulation in 68% of cases and improvement in 12%. Littauer and Wright (Amer

Book Reviews and Notices

BRITISH MEDICINE By R. McNair Wilson, published by William Collins of London with 8 plates in colour and 20 illustrations in black and white, pp 48, price 3s 6d

Dr McNair Wilson is a well-known medical journalist, his life of Sir James Mackenzie, *The Beloved Physician*, is a classic. The development of modern medicine since the Renaissance is astounding, and the part played in this advance by the British doctors is enormous. It is hardly possible to survey this in a small essay of about 30 pages of written matter but Dr Wilson has succeeded remarkably in arousing our admiration for the British Medicine. Per necessity, the essay is a mere outline leaving out many important aspects of British medicine and some masters of physiology, neurology, cardiology and clinical medicine are not mentioned. However though written for lay readers, the perusal of this essay will inspire any student of medicine and fill him with joy at the achievements of so many great workers. The beautiful colour plates of Harvey, Allbutt, Manson and Bruce and the delightful illustrations in black and white of masters of British medicine together with a few Rowlandson cartoons, will in themselves repay the price.

No apology is needed for the title 'British Medicine'. Medicine, like all other sciences, is international, the author recognises this when he says "It is well, therefore, to remember that behind each discovery lie as a rule, a long series of smaller and earlier discoveries, each one which represents an essential part of the completed structure. Banting, for example, could not have discovered insulin if nothing had been known about the island tissue of the pancreas, and so on. Nor can English medicine claim any monopoly of discovery, medicine knows no frontiers and holds no respect of persons. The English claim is rather the consistent presentation of a method which, from generation to generation, has proved its worth and by which the store of human knowledge has been enriched and human suffering in consequence alleviated in all parts of the world"

BRITAIN'S HEALTH By S Meivyn Herbert, with a foreword by Lord Horder Allen Lane, Penguin Books, Ltd, Harmondsworth, England pp 219, 1939, 8 as

This is a condensed report on a more voluminous work produced by P E P (Political and Economic Planning) Its thirteen chapters deal with all the aspects of health and ill-health, individual and national It is indeed an admirable survey and deserving of the highest praise

We wish the National Planning Committee in India will produce something like this for each of the Indian Provinces Our legislators' and corporators' activities about national health appear to be centred round practising nature cures, opening homoeopathic dispensaries, encouraging cheap or free distribution of harmless mixtures by half starving practitioners or a relapse in the past with a pious hope that in 1942, all ills of India will vanish if the writings of the hoary Chaika, Shushutra Bhavamisra or Avicenna were taught to our young boys and girls and if a few lacs of rupees were obtained from the overflowing hoards of speculators to build an imposing stone structure or two The reviewer would suggest a compulsory study of this book by all our legislators and corporators It will show them the complexities of the health problem of a nation, and will perhaps suggest to them the ways and means of creating a health scheme for the varying needs of our country, avoiding the pitfalls in which the English have fallen

To the practising physician, both the individual and the state the book makes an interesting reading The comprehensive nature of the survey is shown by the following chapters selected from the Contents

Ill-health—its cost, Environmental Services, Sewerage, Refuse Collection, Water Supplies, Housing, Atmospheric Pollution, Noise, Food and Drugs Legislation, Patent Medicines The Medical Profession, The Doctor's Job, National Health Insurance, Hospitals, Mothers and Children Professional Health Service, Special Services, Mental Disorder and Deficiency, Tuberculosis, Cancer, Cripples, The Blind and the Deaf, Venereal Diseases, Highlands and Islands, Gloucestershire Medical Service Scheme, Peckham Pioneer Health Centre Building Physique Nutrition, Physical Education, Industrial Health

As Lord Horder states in his foreword, "If the book be read straight through the reader will find it an exciting record of the struggle of sanity in health matters of the ordinary people of the nation Moreover the reading of it will reveal what I consider to be the most striking fact in relation to the National Health situation—the repeated overlap of what we academically term 'health', with economics with poverty, with labour, with housing, with transport, and with agriculture"

We heartily endorse Lord Horder's remarks

Doubtless a people gets the health, as it gets its government which it deserves and whatever the reader's conclusions may be

after reading this book, it remains with himself that the onus of securing efficiency in our Health Service really lies

An individual cannot be said to be "alive" at all, certainly he cannot be "healthy" or "happy", without certain basic needs, such as enough of the right food, decent shelter, a job of work under suitable conditions, opportunity for play and access to sunshine and fresh air. Without these very simple things health and happiness are a mirage. To preach health to the underfed is a hypocrisy."

SCIENCE IN WAR By 25 Anonymous Scientists Allen Lane Penguin Books Ltd Haimondsworth, England pp 144, Second edition 1940, 8 as

It has been said that the present war is a war of Science. Only man-power or blind heroism of a few individuals is of little avail. That Russia, the despised nation of the world, has held its own against the most powerful foe on land, is we have no doubt more due to its scientific development and organisation than to General Winter. During the decade preceding the War, Russia was not idle, was not bound by old shackles. Her young men were creating an organised scientific society. That without scientific organisation and without the full use of all the scientific resources it is not possible to win the present war has dawned upon twenty-five scientists in England, and they have attempted in this booklet to analyse the conditions which led to a dangerous state of affairs by the half hearted use of science in war effort in England. All writers are authorities in their own subjects and the eight chapters in which the book is divided make a stimulating reading. The authors succeed in showing that the scientific knowledge is of immediate and decisive importance to the present world struggle. The main issue of the war and the peace that will follow will largely depend on how effectively and quickly scientific ideas are used by the state. The whole book is an interesting reading but the sections dealing with the abolition of the enteric fevers among the troops and with the control of typhus by energetic delousing and an attack on the ultimate reservoirs of Rickettsia, rats and apparently healthy carriers, and the chapters on the Wounded and Food, practically comprising half the booklet, will be of special interest to the physicians. These two chapters contain a wealth of information and ideas and we heartily commend the book to our readers.

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LIVERGEN

COMPOSITION

Indigenous drugs —

Andrographis Psychotis — I enusreck

Hydrophila, Oldenlandia etc

B P Drugs —

Sodi phosph, Sodi Benzons Cascara

Sagrad and bile salts etc

INDICATION

(1) Bad liver and habitual constipation

(2) Congested and enlarged liver with muddy stools for all ages

(3) Jaundice (Catarrhal)

(4) Hepatitis and other disorders of liver function after amoebic Dysentery Malaria or Kala azar

“ Have not met with a better preparation for defective liver function ”

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Let us remember..

TYPHUS IN HISTORY

Hans Zinsser

(1878-1940)



Hans Zinsser was a bacteriologist of repute, a philosopher, historian, poet and wit. Apart from many articles on original research in medical journals he published *The Text book of Bacteriology* (1911), *Infection and Resistance*, *Resistance to Infectious diseases* (1931), *Immunity* (1939), *Rats, Lice and History* (1935), and *As I remember Him* (1940). He died of Leukaemia. In his autobiography he had forecasted his death in the following memorable passage, which gives some insight into the mind which knows of certain death in near future. Such a revelation shows that there is no point in withholding the truth from the

incurables if they desire to know it.

Something took place in his mind that he regarded as a sort of compensatory adjustment to the thought that he would soon be dead. In the prospect of death life seemed to be given a new

meaning and fresh poignancy. From now on, instead of being saddened, he found—to his own delighted astonishment—that his sensitiveness to the simplest experience, even for things that in other years he might hardly have noticed, was infinitely enhanced.

"As the disease caught up with him R. S. felt increasingly grateful for the fact death was coming to him with due warning, and gradually. So many times in his active life he had been near sudden death by accident, violence or acute disease, and always he had thought that rapid and unexpected extinction would be most merciful. But now he was thankful that he had time to compose his spirit and to spend a last year in affectionate and actually merry association with those dear to him."

There are few diseases whose ravages can compare with those of typhus. From ancient times it has followed in the wake of wars and decimated armies and populations. Between 1917 and 1923 according to Terassewitch, 30,000,000 cases of typhus with 3,000,000 deaths occurred in European Russia alone. Russia, the Eastern Europe, the near East and Malaya States, Formosa, Sumatara, Annam and Japan are endemic centres of typhus fever. In all these fields of war are Indian soldiers and if there is an epidemic of typhus through the breakdown of the prophylactic measures we should be involved in it just as much as anybody else. Hans Zinsser, who investigated the disease in Eastern Europe during the last world war has written an interesting account of the history of typhus in his absorbing book, *Rats, Lice and History*, from which we give the following account—

"Applying modern technical judgment to the accounts of infectious diseases of other times, we can find, in none of the cases that have been cited as example of typhus fever before the twelfth century, trustworthy evidence that the conditions described represented this disease as it is known at the present day. The affliction of the Clasmomenian, the tenth and accurately described case in the First Book of Hippocrates' Epidemics, cited as typhus by Ozanam, appears to us more like a case of typhoid fever than one of typhus. The only description in the Epidemics which strongly suggests typhus is the one of Silenus. Not in Herodotus, Vegetius, Aetius, or Galen, nor in any other ancient writers who are cited, here and there, as having seen typhus in classical and post-classical periods, is there any description from which reliable conclusions can be drawn. We might, from this, with others who have had similar negative experience, deduce that the disease was actually new to Western Europe until shortly before the time of Fracastorius, that it was imported with soldiers from Cyprus, possibly pre-existing in a quiet way in the East. This, as we shall see, however, is not a necessary conclusion.

It will be helpful, before we go into this matter more deeply, to consider the descriptive criteria which justify us in assuming that any disease referred to by historians is actually typhus

Typhus is an acute fever which does not always behave in a conventional manner. In its typical course it occurs more or less as follows. The onset may vary from extreme abruptness to a more gradual one. As a result the initial stages resemble closely those of severe influenza. The temperature rises rapidly often to from 103° to 104° Fahrenheit, with chills, great depression, weakness pains in the head and limbs. The eruption appears on the fourth or fifth day after the onset and, except in times of epidemic, the diagnosis is extremely difficult in the pre-eruptive stage. As the eruption appears, the fever is apt to rise. The rash usually begins on the shoulders and trunk, extending to the extremities, the backs of the hands and feet, and sometimes to the palms and soles. It becomes more abundant during the subsequent days, but it is seen very rarely on the face and forehead. It is at first composed of pink spots which disappears on pressure, but soon these become purplish, more deeply brownish red, and finally fade into a brown colour. These are the "petechiae" and "peticuli" of the older descriptions. A symptom of considerable importance, early and rarely missed, is the severe headache which is apt to be more unbearable in this disease than in other acute fevers, indeed, it is for this reason that one is inclined to assume, though not to assert with certainty, that varieties of the so-called *Kopfkrankheit* or *Hirnentzündung* of mediaeval writers might have been typhus fever. Without the rash, however, and in the absence of an epidemic, the diagnosis of typhus fever would often remain uncertain even today, except for a specific reaction of the blood which was not available until quite recently.

When the rash, together with fever and headache, delirium and extreme weakness, is clearly described, typhus is easily recognized, but it must be remembered that the rash in the mild isolated endemic cases—and especially among children—may be so slight and transient that often it is not noticed at all by the physician unfamiliar with the disease. For this reason until typhus becomes epidemic, individual cases may often remain unrecognized, or may be described in such a general manner that it is impossible to differentiate them from measles,

scarlet and typhoid fever, malaria, and a number of other febrile conditions that were common in ancient and mediaeval times. Certainly that typhus existed in the fifteenth century and later is made possible largely by its epidemic occurrence. Under such circumstances, the description of individual, severe, and typical cases is re-inforced by accounts of the characteristics of the epidemics, seasonal and other accessory factors, manner of spread, and mortality. Taken together, this information furnishes a structure of interrelated clues which permits certainty as to the nature of the disease. We can thus conclude with some confidence that, as an epidemic disease, typhus did not exist in Europe until the fifteenth century.

Until very long ago, typhus fever was thought of as a single, individual disease quite separable from other fevers, and unique. From studies—none of them older than twenty years, and most of them carried on since 1928 we know that typhus fever is the most distinguished member of a family of maladies which are grouped together, for reasons that will be clear presently, under the name of the *Rickettsia* diseases.

Closely related to typhus, quasi in the position of a second cousin is Japanese River Valley or Tsutsugamushi fever. This disease is conveyed to man by the bite of the harvest mite, the *Trombicula akamushi*, and the insect picks up the infection from field mice and rats which are the natural reservoir of the disease. The virus is thus kept alive in endemic regions, by circulation between field mouse and harvest mite, and by the latter it is, on suitable occasions, transferred to man.

A closer relative, let us say first cousin of typhus is the disease—or the group of variants of the disease—called Rocky Mountain spotted fever. The infections properly belonging to this division of the family are conveyed to man by the bites of ticks, and since, in these cases, the virus can be hereditarily transmitted from both the mother and the father tick to the little ticks, no animal reservoir is necessary for continued survival. Yet, since guinea pigs, rabbits, and a number of other animals are susceptible to the disease, it is not impossible that an animal reservoir, as yet undiscovered, may exist.

Probably identical with our American spotted fever is the so-called, tick-transmitted, "typhus" of San Paulo, Brazil. It is an interesting demonstration of the essential similarity of these infections in man that the San Paulo tick fever was re-

garded as true typhus by experienced physicians as long as clinical observations unaided by laboratory study formed the sole criteria of judgment

Another variant of the spotted-fever group is the *Fievre Boutonneuse*, or *Escharo-nodulaire*, which was first described from Provence in the neighbourhood of Marseilles, but has also been found in Rumania. It is tick-transmitted and, as in spotted fever, the virus passes hereditarily from one generation of tick to another, without the necessary intervention of an animal reservoir

Finally, in true typhus fever we now know of two distinct subfamilies, and suspect that others may exist

As in other *Rickettsia* diseases, the virus of both varieties of typhus is transmitted to man by insects. The body and the head louse carry the infection from one human being to another. The louse takes up the virus with infected blood, the *Rickettsiae* multiply in the cells lining its stomach and intestinal walls, and appear in large numbers in the faeces. Louse transmission was the great discovery made by Nicolle, which furnished the first powerful weapon for a counter-attack against the disease. It explained the manner in which epidemics are propagated. It removed all mystery from the historic association of typhus epidemics with wars, famines, and wretchedness. It justified the traditional designations of "camp fever," "prison fever," and "ship fever." But it left unanswered the problem of the persistence of the smouldering embers of the virus in interepidemic periods. For the human louse, probably a relatively recent host of the *Rickettsiae*, is even more susceptible than man. It sickens and dies usually within twelve days, always within two weeks. Where does the virus persist between outbreaks? How are the interepidemic cases engendered?

An approach to the answer to these questions was furnished a few years ago by a study of the isolated cases of typhus which occur every year—here and there—in the United States. These cases occurred under conditions in which louse transmission could be excluded, and a search for other sources of infection was begun. The result was the discovery of typhus virus in rat fleas and then in the rats themselves. The epidemiological cycle seemed complete. Domestic rats carry the infection. In them it is perpetuated by transmission from

rat to rat fleas and by rat lice. Rat fleas will feed on man when driven to see a new host by death of the old one—a frequent occurrence when domestic rats die or are killed. From the bite of the infected fleas the human being contracts typhus. This is the sporadic or endemic case. If the victim is lousy, group infection may result. If he lives in a louse-infected community the consequence is an epidemic.

The extraordinary aspect of the situation is the fact that, in one and the same era, mankind suffers from a group of almost indistinguishable acute fevers, which reach him by a variety of complex parasitic cycles as follows—

Tsutsugamushi	Mite	{ Rat			
Spotted Fever Types	Tick	{ Field Mouse	Mite	Man	
Fièvre Boutonneuse	Tick	{ Flea	Man		
True Typhus		{ Dog	Tick	Man	
Murine Type	Rat Flea	} Rat (Mouse)	{ Rat Flea	Man	Louse
	Rat Louse				
European (Human) Type	Man		{ Louse	Man	

There are two distinct types of true typhus virus. The diseases they cause in man are identical and both are transmitted from one individual to another by human body and head lice. Both in man and in animals recovery from one type protects against the other, testimony of their close and fundamental kinship. They can be distinguished only by relatively slight but definite differences of behaviour when inoculated into guinea pigs, rats and mice, and by immunological reactions. Before these distinctions had been recognized typhus had been regarded all over the world as a single disease perpetuated by man-louse-man transfer. This observation, however, together with epidemiological observations in Australia and American case studies, led to an intensive search for virus reservoirs other than man. The result was the discovery of natural rat infection and of rat-flea transmission.

Now in correlating the origin of virus strains with their manner of behaviour in guinea pigs, it was soon observed that all the viruses obtained either directly from rats or from rat-fleas, as well as those isolated from human victims in America and Mexico (regions where the presence of infected rats and epidemiological circumstances indicated rat origin), behaved in one way, while the strains obtained from man in South-

eastern and Eastern Europe—where endemic and epidemic typhus has been prevalent for centuries—behaved in another manner. For these reasons students of the disease to-day classify the two varieties as the “murine” type—in which the rat-flea cycle precedes human infection—and the classical or “human” type, for which no rat origin has as yet been determined. The precise relationship between these closely allied sub-varieties then became the focus of attention, since it was obvious that comprehension of this would go far toward explaining the epidemiology of the classical European disease thereby furnishing new principles for protective measures. The speed with which things have been moving in the typhus world may be gathered from the fact that most of the work we are discussing has been done since 1928, a good deal is hardly off the presses, and some of it is not yet in print as these paragraphs are being written. In its accomplishment, French, Swiss, American, British, German, Mexican and Polish investigators have engaged in the sort of exciting, friendly, and eager competitive collaboration or collaborative competition which gives our profession a zest and charm and a freedom from nationalistic chicane found in few others.

We can assume with much confidence, therefore, that the two varieties are fixed, though very closely related, variants. But the ease with which one of them can temporarily be trained in the direction of the other by experimental manipulation suggests that the differentiation is one that has come about, biologically speaking, at a relatively recent period. Some light on this phase of the matter has come from accidental observations made on strains obtained in Mexico. Now and then, from one and the same Mexican epidemic, among typical murine strains, a few aberrant ones have been recovered which act like the European or human variety. Some of these may retain their human strain characteristics through many guinea-pig passages. Eventually, however, all of them, especially under the influence of rat passage, have “come back” to the murine attributes. Since the Mexican epidemics the passage from man to man—just as in the Continental epidemics—is a louse transmission, the observation just cited suggests that passage through man and lice tends to modify the properties of the murine virus into a closer similarity to those of the European human type.

Saracens. However this may be, the physicians of that time believed that the spotted fever was contagious and identical with plague.

The disease of which we are speaking was disseminated from the camps of Granada to the army of Don Fernando, the Catholic. Whether for this or some other cause, when the army was reviewed at the beginning of the year 1490, the generals noticed that 20,000 men were missing from the rolls, and of these 3,000 had been killed by the Moors and 17,000 had died of disease, not a few of them succumbing to the severe cold—a kind of death which says Mariana, was very miserable.

There can be little question that this was typhus fever, and one of the most interesting parts of the passage is that in which the origin of the infection is referred to “certain soldiers who came to the war of Granada from the Island of Cyprus, to which island this disease is peculiar.”

In the second paragraph the disease is credited with having killed 17,000 soldiers, as against the 3,000 killed at the hands of the Moors.

In the next passage, which deals with the epidemic of 1557, Villalba again indicates that the disease was newly imported at the time of the civil wars for Granada. By this time, epidemics had spread over the entire Spanish peninsula and raged, unchecked, for thirteen years, until 1570 —

A new disease, unknown until the time of the civil wars in Granada, appeared in Spain in the year 1557 and depopulated the greater part of our peninsula, it did not begin to decline until the year 1570. This new pestilence was believed to have originated among the Saracens after the war of Granada, that is, after the King Don Fernando of Aragon and Dona Isabel, Queen of Castille, conquered that city, and after the Moors had been dispersed by the decree of Don Felipe II. That this infection came from the Spanish Arabs can be deduced from the fact that almost all those who were driven from their homes infected, by association and contact, the inhabitants of the villages, towns, and cities, as related by Luis de Toro in his treatise on Spotted Fever, in this work may be found his description of the

character of the disease as it occurred in the periods 1570 and 1577

The disease was thus well launched in an epidemic form in Europe during the last decade of the fifteenth century and throughout the sixteenth, but had not yet spread widely across the Continent. In 1546 Fracastorius published his *De Contagione*, in Chapter VI of the Second Book of which he gives an excellent description of the disease in its clinical appearances and has many sagacious things to say about its nature and the manner of its spread

Before the middle of the sixteenth century typhus fever had begun to take an active hand in the politics of Europe. It made its political debut as one may call it, by one of the most far-reaching and profoundly effective strokes of its entire career, plying the decisive role in the relief of the Imperial army at Naples when besieged by the French under Lautrec in 1528.

There followed the sack of Rome—one of the most dreadful calamities that, in its long history, had befallen the Sacred City. The Pope was made a prisoner. The conditions in the city were described by a Spaniard, Villa, as follows: "In Rome no bell sounds, no church is open, no Mass is read. There are no Sundays and no holidays. The rich shops of the merchants are used as stables, the most beautiful palaces are devastated. Houses burn, and the streets are heaps of manure. The stench of the corpses is dreadful, and in the churches I have seen dead bodies gnawed by dogs. Mercenaries are dicing for heaps of ducats in the streets. I can compare it to nothing that I know except destruction of Jerusalem." The captivity of the Pope was dreadful, not only for physical suffering and anxiety, but also because it was aggravated by an outbreak of plague which came with the summer and killed enormous numbers of the citizens, including many of those immediately attached to the Pope's persons. Two cardinals, imprisoned with him, died of the disease, which was probably bubonic plague.

The same disease—contracted in Rome—killed Lannoy, the Imperial general. The death of this energetic leader probably had a good deal to do with the subsequent initial successes gained by Lautrec who led the French troops that were now

approaching Northern Italy At first, the advance of the French was a triumphal march

It is impossible to estimate the consequences for the future history of Europe if Naples had fallen at this time with Italy and the Pope ready to acknowledge Francis I as liberator and defender of the faith—but then came Typhus On July 5, Lautrec had believed Naples incapable of resisting any longer, but in the marshy, crowded camps of the French the pestilence was destructive and rapid Within thirty days, more than half the army died, according to some accounts, of 25,000 men only 4000 remained Vaudemont, Navarro and Lautrec himself were taken sick and died Their successor, the Marquis of Saluzzo, realized that the siege must be immediately raised On a rainy night of the twenty-ninth of August, the retreat began, closely followed by the energetic Prince of Orange with his cavalry The remnants of the French army were cut to pieces They were murdered or disarmed, to perish later at the hands of the peasants A few bands managed to reach Rome, half naked and sick Charles V was crowned ruler of the Roman Empire at Bologna by the power of Typhus Fever

North America, Mexico

- 1116 A D — destruction of the Toltec City of Tollan by typhus epidemic
- 1545 A D — epidemic of typhus in Tlascala killing over 150,000 Indians, 100,000 in Cholula, and a similar mortality in other provinces
- 1564 A D — Aztecs decimated (Tabordillo)
- 1576 A D — Widespread epidemic in Mexico

Europe

Spreading from Spain to Italy, France and the Northern countries

- 1528 A D — Siege of Naples—Typhus epidemic in the army
- 1552 A D — Siege of Metz—abandoned by Charles V because of a serious typhus epidemic
- 1542 A D — Hungary—30,000 Germans killed by typhus in the army of Joachim
- 1566 A D — Maximilian II—abandons his campaign because of a severe epidemic of typhus in the army From the

army it spread throughout the country and has been right upto the present times endemic in Hungary, the Balkan States, Poland and Russia

1600-1648—Widespread epidemics—to the end of the Thirty Years' War When the Thirty Years' War was ended no corner of the European Continent was left without its foci of typhus infection

1087-1650—Typhus was present throughout the British Isles, known as Famine Fever or Gaol Fever Thomas Willis, the Oxford anatomist has left a description of the disease which decimated both the Parliamentary and the Royal armies at the siege of Reading in 1643 And a similar epidemic in 1650 converted the whole island into one vast hospital

Throughout the eighteenth century the disease raged in its epidemic form in the European armies and the cities It reached its culmination in 1816 to 1819, when it killed 700,000 persons in Ireland In the Franco-Prussian war of 1870 there was no typhus epidemic For some unexplained reason, typhus epidemics declined after 1850, and during the decade preceding the First World War it was leading the quiet bourgeois existence of a reasonably domesticated disease, sporadic cases and localized epidemics occurring in China, Mexico, North Africa, the Near East, Ireland, Russia, Poland and Eastern Austria In North America it existed in a different form described as Brill's disease

In 1909 Charles Nicolle made the remarkable discovery of the louse transmission of typhus fever from man to man For the first time in all the centuries of a one sided warfare, with man forever in the open, and typhus ever in ambush, the victim was in a position to organize a rationally planned and strategically sound defence against his historic enemy

At the beginning of the First World War (1914-1918), typhus began to show itself in the Serbian army in November It is probable that it occurred, at the same time, among invaders In addition to their own troubles the Serbs now had about 60 000 to 70,000 prisoners on their hands, some of them sick and wounded They were short of shelter for their own dispossessed civilian population, there were no adequate quarters for their prisoners Most of their able-bodied adults

were with the colours. There were less than four hundred doctors in the country, almost all of whom sooner or later contracted the disease, 126 of them fatally. The few existing hospitals were soon overflowing, and others had to be improvised in buildings which often lacked sanitary provisions of all but the most primitive order. There were practically no nurses. There were no beds, no linen, no medicines. Eventually there were hardly enough grave diggers. It is impossible to state, with any accuracy, just where the epidemic started. The first accumulation of cases occurred among Austrian prisoners at Valjevo. Dissemination to all parts of the country was almost immediate. The infection travelled with the wandering population, with prison trains, and with moving troops. Through February and March the epidemic flared up with a speed and violence never equalled in any typhus outbreak of which we have reliable record. In April—when it reached its culmination—the new cases per day ran into many thousands. For a time 2500 were daily admitted to the military hospitals alone. The mortality ranged from approximately 20 per cent during the rise and decline to 60 and even 70 per cent at the height of the epidemic. In less than six months over 150,000 people died of typhus. Not less than one half of the 60,000 Austrian prisoners succumbed.

Typhus from now on took over its historic role along the entire Eastern front. It flourished as usual in all the Eastern armies, but was kept, by extraordinarily effective sanitary measures,—bathing and delousing,—within reasonable bounds among the Austrians and Germans. Though it penetrated into the prison camps in Central Europe, it was successfully prevented from spreading to the civilian populations. Among the most remarkable phenomena of the war is the total absence of typhus from the Western front. No completely satisfactory explanation for this can be offered. Soldiers in the trenches on this front were as universally lousy as soldiers have always been. And a louse-borne disease, Trench fever, closely allied to typhus, was common. We can attribute it only to the fact that the armies were—on both sides—more afraid of typhus than they were of shot and shell. The Central Powers, realizing that a typhus epidemic, introduced with troops transferred from the East, would lose them the war, took the utmost precautions to avoid this. And army sani-

tary organizations, in all the forces, were ever conscious of the possible peril, alert for suspicious cases, and usually quick to resort to wholesale delousing. The mortality of lice in this war must have been the greatest in the history of the world.

In Russia alone did typhus attain its mediaeval ascendancy. During the first year of the war only about 100,000 cases occurred in Russia. After the retreat of 1916 the recorded number rose to 154,000. From then on, for obvious reasons, figures are unreliable, but there is no question that the disease increased steadily and rapidly. Revolution, famine, epidemics of cholera, typhoid, and dysentery, helped. There are no words to record the dreadful sufferings of the Russian people from 1917 to 1921. We are concerned with typhus alone. And from the careful and conservative calculations of Tarassewitch, it is likely that during these years, there were no less and probably were more than twenty-five million cases of typhus in the territories controlled by the Soviet Republic, with from two and one-half to three million deaths.

We have said nothing of the epidemics in Poland, Rumania, Lithuania, and the Near East, but we are—and the reader surely is—weary with horrors. Moreover figures, when they begin to approximate those of President Roosevelt's expenditures, begin to anaesthetize the mind and lose effect.

The methods of attack by typhus are being revealed and appropriate weapons to repulse him are being forged. In this—unlike most other matters of international interest the whole world has co-operated against the common enemy. French, Swiss, American, British, German, Brazilian, Japanese, Chinese, Russian, and Mexican investigators have worked together, cheered each other on and helped one another in friendly rivalry.

Typhus is not dead. It will live for centuries and it will continue to break into the open whenever human stupidity and brutality give it a chance, as most likely they occasionally will. But its freedom of action is being restricted, and more and more it will be confined, like other savage creatures, in the zoological gardens of controlled diseases."

Original Contributions

OBSERVATIONS ON HIGH BLOOD PRESSURE

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It was in the year 1893, that Von Basch of Vienna with the use of his newly invented sphygmomanometer brought to the notice of the medical profession for the first time the clinical entity non-renal or Essential Hypertension, he could not possibly have realized at that time the true worth of his discovery to the medical world. In spite of the massive literature that has grown steadily during the last forty years or so on the subject of hypertension one can truthfully state that the "sum-total of our present day knowledge of hypertension amounts to very little. There is no conformity of opinion even about the nature of hypertension. Whether it is a clinico-pathological entity or merely a symptom-complex shared by a variety of disorders remains undecided, though of late, medical opinion has been inclined to favour the latter view. The aetiology of hypertension remains "shrouded in mystery", its consideration leads us into a veritable "maze of theories" and opinions, from which we emerge as mystified and ignorant as ever. Every few years a new theory is propounded which offers hope of a final solution to this complex problem, just when the enthusiasm of the profession attains its peak and the solution appears "at hand", flaws in the theory are described, opinions clash, opposition grows and one more theory is squashed or rejected. Such a process has been repeated on so many occasions in the case of High Blood Pressure that the profession has now learnt to be more cautious in the acceptance of new theories. Such a cautious attitude on the part of the medical profession is responsible for the relatively scant attention that has been accorded to the masterly work of Goldblatt and his associates, who by means of clamping experiments on the renal arteries of dogs, have

evolved a simple and yet consistent method of inducing persistent arterial hypertension. Their work goes a long way towards proving an important role for the kidney (through an intermediary pressor substance viz renin) in the aetiology of essential hypertension.

The clinical manifestations of hypertension are so numerous, involving as they do practically every organ and tissue of the body, that mere enumeration of these would take up most of our time. I will therefore only deal with a few of those phenomena in which I have taken particular interest.

In this connection, I may state that to detect hypertension in the stage of symptoms and physical signs, as is usually done, is like diagnosing cancer of the stomach in its palpable or inoperable stage, in both cases, the results of treatment are disappointing for diagnosis has been deferred too long. Much more important than an appreciation of the symptoms and signs of hypertension is an early detection of the disease in its so-called "asymptomatic", "prehypertension", "silent", "pre-sclerotic" or "functional" phase, I prefer to term this phase the "presymptomatic" "latent" or better still the "spastic" phase of hypertension. An investigation into the blood pressure and associated pressure phenomena in normal children of school age, undertaken by me two years ago, has been rewarded by the detection of abnormal pressure phenomena (like high systolic and diastolic indices, hyperreactive response to cold, to forced breathing and other stimuli) in a percentage of apparently normal subjects. It has been suggested by various observers, especially in America, that individuals exhibiting such phenomena in childhood are potential hypertensives. The "hyperreactors of to-day are probably the hypertensives of tomorrow." If such is indeed proved to be the case then we can consider ourselves on the threshold of a great discovery, for early detection of the disease in its asymptomatic phase would mean early treatment and probably complete cure of the dreaded malady.

Of the many symptoms of Hypertension, I propose to deal first of all with certain anomalous forms of chest pain or anginal pain encountered in subjects of high blood pressure. There is no doubt that the subject of chest pain has been by no means adequately explained or exhausted. There is need, not

only of a good classification of this symptom but of a clarified clinical study of its various forms. With the classical form of Angina Pectoris, described by Heberden in a lucid manner over a hundred and fifty years ago the average clinician is quite conversant. There are however, anomalous forms of angina, the so-called "formes frustes" of angina, which present considerable difficulty in diagnosis, taxing the clinical acumen of the physician to the utmost. It is to such forms of angina that I particularly wish to direct your attention to-day.

There is the so-called "Angina of Rest" or "angine de decubitus" which probably corresponds to the "spasmodic angina" of Geoffrey Bourne. It differs from Heberden's angina in arising spontaneously or in the absence of physical or mental effort, it may wake the patient up from sleep. To my mind, angina of rest is not one clinical entity but a collection of distinct clinical syndromes amassed together under one designation —

(1) Some of these cases are merely examples of minor attacks of coronary occlusion or thromboses, due to blockage of some small coronary twig. Attacks of pain intermediate in character between angina pectoris and coronary occlusion have been described recently by Levy and Bruenn under the designation of "acute coronary insufficiency", they attribute these attacks to "occlusion of small coronary twigs".

(2) Some cases are merely examples of advanced angina pectoris, where the disease has advanced sufficiently to allow apparently insignificant stimuli like "cold bed clothes" or a "draughtly room" or the effort of "turning in bed" or "undressing", to provoke typical attacks of pain.

(3) McWilliams has demonstrated sudden rises of blood pressure and pulse rate during sleep disturbed by nightmares, on the other hand, during quiet sleep the blood pressure and pulse rate tend to fall. Nocturnal attacks of Rest angina are probably examples of angina of effort, where the effort element is supplied by a rise of blood pressure and pulse rate, both tending to increase the work of the heart.

(4) Lewis has described a special form of anginal syndrome of a vaso-motor type in young and middle-aged males with rheumatic or syphilitic aortic regurgitation. The patient

usually wakes up with the attack in the early hours of the morning, there is profuse sweating violent pulsation in the neck and chest, blushing of the face and a rise of blood pressure and pulse rate, the attack usually lasts from a few minutes to half an hour or more and may be provoked by food or even by "the thought of food"

(5) The "spasmodic angina" of Geoffrey Bourne probably belongs to this group. He has recently published a lucid account of this clinical condition which tends to occur in association with hypertension specific aortitis and aortic regurgitation and is particularly common in doctors, school masters and clergymen. It differs from "effort-angina" in several respects. It does not bear a "quantitation relationship" to exercise as in effort-angina, it is not relieved by rest, it is more severe and prolonged than effort-angina, it is accompanied by sweating, nausea, vomiting and pallor and tends to occur in "highly-strung" individuals.

Another type of anginal pain which is by no means rare in hypertension or disease of the aorta, has been described by German workers under the designation of Aortalgia.

Last year, I published in the Indian Medical Gazette a description of several cases of this type, observed personally. Up to date, I have Case Records of about twenty cases of Aortalgia. Though, at first sight no different from classical angina, Aortalgia displays certain characteristic qualities, viz (1) It tends to radiate into both arms or shoulders. (2) Radiation of pain seldom extends beyond the level of the elbow. (3) The primary chest pain in aortalgia is located high up, under the upper third of the sternum. (4) Subjective feeling of anxiety or 'angor animi' is not experienced. (5) The brachial plexus on the left side is tender to digital pressure during attacks of pain as first described by Schmidt. (6) A band or zone of hyperaesthesia or hyperalgesia appears in the left interscapular region at the back during attacks of pain. (7) Attacks may last for minutes or hours. (8) Sequelae such as feelings of tingling and numbness are common and persistent. (9) Electrocardiography does not reveal any characteristic pattern during these attacks.

Another atypical form of anginal pain that I described in the Indian Medical Gazette some months ago under the designa-

tion of "Xiphisternal Ache" or "Low substernal pain" is characteristically observed in hypertensives with unduly sensitive nervous systems. It displays certain interesting characteristics, viz (1) The pain is located behind the lower third of the sternum or xiphisternum (2) In character, the pain is usually described as "aching" or "like a lump" in the chest (3) The intensity of the pain is seldom intense or unbearable (4) There is no tendency for the pain to radiate in any direction (5) The pain lasts for anything from two minutes to several hours (6) There is an associated tenderness to pressure over the xiphisternum (7) Pain is usually precipitated by worry, depression or emotional upset (8) Pain is often accompanied by emotional outbursts, fits of crying, depression or restlessness (9) There is no associated feeling of constriction or "angor animi" (10) Attacks of pain usually cease spontaneously and often fail to respond to nitrites. Three factors appear to play a part in the genesis of this form of chest-pain viz (a) Organic heart disease, which is usually secondary to high blood pressure, (b) a hypersensitive nervous system and (c) a transitory rise of arterial blood pressure. During the last two years, I have come across no less than thirteen cases of this type. Xiphisternal ache appears to be a forme fruste or anomalous form of angina pectoris.

Acute Transitory Cerebral Episodes or Transient Cerebral Ischaemic Crises.

I would now like to refer to certain transitory or evanescent cerebral episodes which are observed with fair frequency in cases of hypertension. Paullen, Bowcock & Wood described "transient cerebral phenomena" in 112% of their hypertension cases. These attacks "mean" to the brain what angina pectoris means to the heart. In both, the essential pathogenetic defect is a "relative ischaemia" of the parenchyma of a vital organ, in one case ischaemia affects the substance of the heart while in the other it affects that of the brain. In order to stress this similarity further, we might refer to these cerebral phenomena as "angina of the brain".

Transitory cerebral episodes appear under diverse guises. Though, in a few cases, they have been proved to be secondary to minor thrombotic occlusions of the cerebral blood vessels, in the great majority of cases they are due to disturbances of

the cerebral circulation. A perusal of the literature on this subject proves confusing. These attacks have been described under numerous designations, e.g. Cerebral vascular crisis (Pal), Angiospastic insults (Kauffmann), Cerebraleclipses (Donzelot), Acute uraemia and False or Pseudo-uraemia (various authors). The most favoured designation for these attacks at the present time is "Hypertensive encephalopathy" a term coined by Oppenheim and Fishberg in 1928.

Originally, these cerebral attacks were ascribed to renal dysfunction. Though they do bear a certain clinical resemblance to Uraemia, the resemblance is superficial and does not bear scrutiny. Volhard has convincingly proved the non-renal origin of these attacks by a study of the blood-chemistry and renal function tests. He has dispelled from our minds once and for all erroneous notions about the "renal origin" of these attacks, the terms "acute uraemia" and "pseudo-uraemia" have therefore rightly been discarded from current medical literature.

The term "Acute hypertensive encephalopathy", in vogue at the present time, is not entirely free from defects. Though convenient in practice it is nevertheless open to criticism. For instance, (1) the term "hypertensive encephalopathy" makes no reference to the essential pathogenetic factor of these attacks, viz ischaemia or anoxaemia of the brain-parenchyma. (2) It gives the impression that hypertension is an essential or constant feature of these attacks, though such is indeed the case in the majority of attacks, it is well to remember that there are exceptions. On more than two occasions, I have witnessed typical attacks of this nature in the absence of all hypertension, the blood pressure was perfectly normal in these cases during and after the cerebral episodes. It is possible that in these exceptional cases, the vaso-constriction or angio-spasm might have been confined to the cerebral vascular tree. Such a "regional spasm" of peripheral blood-vessels, if it occurs, would explain the existence of cerebral attacks in spite of normal arterial blood pressures. (3) The term is exclusive of the condition of "Relative Hypotension" (Stieglitz), where sudden fall of blood pressure induces similar cerebral attacks by causing anoxaemia of the brain substance. (4) The term fails to denote the transitory or evanescent character of the attacks, a feature of great importance in diagnosis. (5) The word encephalopathy

directs attention to the brain-substance rather than to the cerebral circulation. These attacks are due not to disease of the brain substance but to defective circulation. With these objections to the above-mentioned term in mind, I make bold enough to suggest what to my mind appears, a more convenient and accurate designation for these cerebral attacks, viz "Transitory Cerebral Ischaemic Crises", an alternative term suggested is "Acute Transitory Cerebral Ischaemia". These terms possess the following merits, they stress (1) the acute or sudden onset of the attack, (2) the transitory or evanescent character of the attack, a feature of diagnostic value, (3) the important role of cerebral ischaemia in the genesis of the syndrome and (4) they do not demand the co-existence of high blood pressure.

Clinical Forms

These are so numerous and varied that I can only enumerate the important types. I have found the following classification satisfactory in practice —

(1) The *epileptiform type* of attack. This constitutes the full-fledged syndrome of hypertensive encephalopathy, which is seldom observed in hypertensives, it usually occurs in the course of acute glomerulo-nephritis. The attacks are clinically indistinguishable from those of major epilepsy.

(2) The *amaurotic form* of attack, with sudden onset of blindness or defective vision in one or both eyes. The attack may last for hours or days. Ophthalmoscopic examination reveals either a normal fundus appearance or spasm of the retinal arteries.

(3) The *syncopal form* of attack. I have been fortunate enough to witness this form of attack in two hypertensive cases within the last four weeks. In both cases, attacks were observed "after a hard day's work". During the attack, the patient would either become dazed or unconsciousness for about an hour, the arterial blood pressure and pulse rate would rise to high figures, a little twitching of the fingers was observed during the attack on two occasions.

(4) The *paralytic form* of attack, with loss of power. This may take the form of hemiplegia, monoplegia, bulbar palsy or facial weakness. In a case observed by me recently, hemi-

plegia occurred about five times in twelve hours and finally became permanent

(5) The *aphasic form* Aphasia either motor or sensory may arise spontaneously and last for hours or days One of Osler's cases had twenty attacks of aphasia of this type

(6) The *psychotic form* where mental symptoms e.g. acute maniacal excitement, stuporose states, auditory and visual hallucinations, arise suddenly and last for hours or days

AETIOLOGICAL CLASSIFICATION of Acute Transitory Cerebral Ischaemia

The one pathogenic factor, which can be considered common to all cases is "ischaemia" or deficient supply of nutritive material to the brain

Considerable evidence has been amassed in support of this theory Post-mortem examination in these cases of so-called hypertensive encephalopathy practically always reveals pallor or anaemia of the brain with or without cerebral oedema ("wet brain" or dry brain" of Cohnheim) Kussmaul & Tenner were able to induce in animals epileptiform attacks closely similar to those of "hypertensive encephalopathy" by experimental ligation of cerebral arteries and artificial production of cerebral anaemia Cerebral ischaemia may arise in one of three ways (1) from *spasm of cerebral blood vessels* This may or may not be accompanied by peripheral vaso-constriction elsewhere, generalized vaso-constriction elsewhere will mean a rise of arterial blood pressure (2) from *exudation of fluid* into the brain-substance viz cerebral oedema Accumulation of fluid leads to compression of the cerebral blood vessels (3) from fall of arterial blood pressure, *relative hypotension* When the blood pressure in a confirmed hypertensive suddenly attains low values, then cerebral phenomena are often induced The fall of pressure may be due to relaxation of peripheral arteriolar spasm or to a drop in cardiac output According as to which of these mechanisms comes into play, we can tentatively classify "acute transitory cerebral ischaemia" into 3 main types

(1) The *Angio-spastic or vaso-constrictive type* The aetiological factor concerned is spasm of the cerebral blood vessels This factor has been held responsible by "

resistance. In any case, the clinical picture is that of Asystole Gauche or Left-sided failure.

Dyspnoea, paroxysmal or continuous, is the symptom par excellence of this type of failure, cough with "rusty-brown" or "chocolate" coloured expectoration is commonly observed in elderly hypertensives. Crepitations are audible over the lung bases, the second heart sound becomes accentuated in the pulmonary area and gallop rhythm and pulsus alternans, the two classical signs of "myocardial exhaustion" make their appearance. Fluoroscopy usually reveals a "boot-shaped" heart with pulmonary congestion. The venous pressure is normal in most cases. As regard circulation time, the "lung to tongue time" which is obtained by deducting the "arm to lung" or either time from the "arm to tongue time," is nowadays regarded as the best measure we have of the "functional capacity" of the left ventricle. In my series of left ventricle failure cases, the "lung to tongue" time was found to range from 7 secs to 14 secs with an average of 9.7 secs.

Amelioration of symptoms in cases of left-sided failure does not necessarily mean clinical improvement, paradoxically enough, it may portend the advent of right ventricular failure in some cases. When failure of the right ventricle sets in during the later stages of hypertensive heart disease, the clinical picture of right ventricular failure is superadded. We get a "mixed form" or "combined form" of heart failure, where signs and symptoms of systematic and pulmonary congestion are intermingled. The clinical picture of "mixed failure" is not constant, it presents diverse combination of symptoms and signs. There are two or three forms of "mixed failure" with rather distinctive clinical pictures, which I would like to draw your attention to.

Bernheim's Syndrome represents a type of cardiac failure, which is common enough in hypertensive subjects but practically unknown to the majority of physicians. Attention has been directed to this syndrome by Bernheim of France and Fishbein of America. In this syndrome, one observes a unique combination of signs, the hypertensive state is associated with a full-fledged picture of right sided failure and few if any signs of left-sided failure. Oedema, venous engorgement and

hepatomegaly are conspicuous, crepitations may be audible at the lung bases, the pulmonary second sound is normal

Many views have been expressed in an attempt to explain right sided failure in cases of hypertension. Bernheim has attributed the syndrome to gross hypertrophy of the inter-ventricular septum with resultant partial obliteration of the right ventricular chamber. It is possible that in some of the cases of Bernheim's syndrome the aetiological factor responsible may be disease of the right coronary artery or emphysema. Bernheim's syndrome is common in youthful hypertensives, as shown by Fishberg.

Another type of failure occasionally encountered in cases of Hypertension is the Asystole Hepatique, where the main brunt seems to fall on the liver. A conspicuous feature of this type is the large and tender liver with ascitis, occasionally associated with splenomegaly.

Another type of failure encountered is the Pericarditic Form which bears a clinical resemblance to the entity described by Paul White under the designation of Chronic Constrictive Pericarditis. The main features are (1) a tender and large liver, (2) a rapidly recurring ascitis, (3) a severe degree of venous engorgement, (4) oedema of the lower extremities and (5) a normal blood pressure.

It is distinguished from Paul White's disease by (1) enlargement of the heart and (2) by lack of evidence of calcification in the pericardium.

Case Reports

A CASE OF TYPHUS

By B R PATEL

M B B S, B M S
BOMBAY

V S M, male aged 27 was seen by me on 2-3-41 for fever, headache and bodyache of two days duration. That morning his temperature was 100.5°F and pulse rate 96 per minute. In the evening the temperature was 102.5°F and pulse rate was 100 per minute. During the next few days he complained of joint pains but there was no swelling of the joint or limitation of movements.

On the 4th day of fever a pink rash appeared on his forearms and legs. During the next two days the rash became more marked and distinctly visible on the patient's fair skin, being more or less equally distributed on forearms, hands, legs, abdomen and back, and well marked on the wrists, palms and feet. It was less marked on the abdomen and chest and the face and neck were free. The efflorescences were quite discrete. The macular and maculopapular rashes were pink in colour, and faded on pressure, while the ecchymotic ones were purple in colour and failed to fade on pressure.

Nothing abnormal was detected in the heart, lungs and nervous systems. The tongue was slightly furred. There was severe headache.

In the first week the temperature was more or less continuous, being 101°F to 102°F in the morning and rising upto 104°F in the evening, and the pulse rate varying from 95 to 105 per minute. In the second week the temperature was swinging from 99°F in the morning to 105°F in the evening, the rise was accompanied by a chilly feeling but no rigor. In the latter part of the second week and the early part of the third week there was a double rise of temperature, being 99°F at 8 a.m., 104°F to 105°F at about 2 p.m., 99°F at about 5 p.m. and again 103°F to 104°F at about 9 p.m.

During the second week the headache was present but severe only when the temperature was high. During the third week the temperature kept low and touched normal on the twenty-first day, the pulse rate coming down to 84. The patient had an uneventful recovery.

During the second week the rash showed no definite changes. But in the third week the macular and maculopapular non-petechial rashes gradually faded, but the ecchymotic ones remained visible by brownish pigmentation. The pigmentation persisted for about three months after the temperature touched normal.

Blood Examination

- (a) Widal for typhoid paratyphoid A and B, negative on the 10th day and the 16th day
- (b) Blood culture on the 14th day, negative
- (c) Leucocytes
 - (1) On 3rd day Total leucocytes 6950 per cmm
Differential Poly 60%, Lympho 36%, Eos 1%, Large mono 3% No malarial parasites detected
 - (2) On the 5th day Total leucocytes 8150 per cmm
No malarial parasites detected
 - (3) On the 13th day Total leucocytes 18250 per cmm
Differential Poly 70%, Lympho 28%, Eos 1%, Large mono 1%, No malarial parasites detected

The interesting points in this case are the following —

The patient was a resident of Ahmedabad, he had been to Bangalore for about a fortnight and while returning from Bangalore he stopped at Bombay, for about a week, during which he fell ill and was compelled to stay at Bombay as a guest of his friend

As typhus is rare in Bombay, and the symptoms were not so severe as described in the text books, the case was not diagnosed as typhus even though a few specialists were consulted. It remained a mystery for nine months, till in January 1942, when I came across an article on "Endemic Typhus in Mysore" by Heiling and Naidu in the December 1941 issue of the Indian Medical Gazette, wherein typhus is stated to be endemic in Mysore, and the clinical features of my case resemble those of the case reports in that article. As my patient had stayed for about a fortnight in Bangalore and had visited various places in Mysore he must have been infected there and developed the symptoms in Bombay.

Note In cases of obscure toxic states, where typhus is suspected blood films, repeated complete red and white blood counts, haemoglobin estimations, blood cultures and if there is a meningeal reaction, lumbar puncture are essential in order to exclude other diseases. The *dialo-reaction* is stated to be invariably and markedly positive at the onset of typhus fever. **Wilson-Weil-Felix Reaction** From the beginning of the second week or a day or so earlier, the serum of a patient suffering from louse typhus is found to agglutinate suspensions of the *B. proteus* X19 (o-cultures o > 19) being used). The *B. proteus* X19 was originally isolated from the urine of typhus patients. It is, of course not causal of the disease and the reaction is probably a para-agglutination phenomenon. With the exception that cross-agglutination of *B. proteus* OX 19 occurs with sera derived from cases of louse typhus and murine typhus, the reaction is specific. Agglutination in a dilution of at least 1 in 200 is necessary for diagnostic purposes. The titre rises, and near the end of the attack may exceed 1 in 600.

Critical Notes and Abstracts

SUDDEN DEATH IN MYOCARDIAL INFARCTION

George Leroy and Sinclair Snider have studied clinically and experimentally the cause of sudden death of patients with few symptoms of heart disease (J.A.M.A., Dec., 13, 1941, pg 2019). They found that the heart of a victim of sudden death rarely fails to disclose lesions in one or more of the coronary arteries which impede or obstruct the blood flow. In location and extent these lesions often cannot be distinguished from similar ones found in patients dead from other causes. The myocardium of a victim of sudden death nearly always contains an infarct. The infarct may be of any size and in any position, in this respect it differs in no way from a fibrous scar of a healed infarct that is seen so frequently in the post mortem room. In an effort to explain the paradox that presumably identical cardiac, vascular and muscular lesions may or may not cause sudden death, most writers have assumed the intervention of some sort of a reflex disturbance of cardiac function, severe and sudden enough to prove fatal. Ventricular asystole and ventricular fibrillation have been demonstrated as the terminal mechanism in the few instances in which electrocardiograms were being made when death occurred. The majority of patients died with ventricular fibrillation, but the mode of its development has not been clearly understood. Leroy and Snider performed many experiments on the dogs to understand this reflex, and to modify the incidence of sudden death after experimental coronary artery occlusion. Their work suggests that subsequent to the myocardial infarction there is a generalized coronary vasoconstriction. This ischemia of the myocardium, provoked by a reflex coronary vasoconstriction, causes ventricular fibrillation in the myocardium which is susceptible to the development of this arrhythmia. The main pathways of the reflex are—the afferent impulses from a myocardial infarct travel centrally through the cardiosensory nerves, the stellate ganglions and the upper thoracic sympathetic ganglions. The efferent impulses provoking vasoconstriction must travel from the brain to the coronary arteries in the vagus nerves since they are the only generally accepted conductors of such activity. The denervation of cardiosensory nerves prior to infarct in experimental animals reduces the mortality strikingly. Bilateral removal of the stellate ganglions and the upper five thoracic sympathetic ganglions reduces the mortality in conscious dogs from a control value of 75% to only 10%. The realization that reflex phenomena are responsible for the sudden death of a patient with myocardial infarction is very valuable. Appreciating this, one should be less prone to pass over lightly mild symptoms, which may be the only evidence of an infarct that can at any moment initiate fatal ventricular fibrillation. The experiments have again a therapeutic significance. The authors found

that amelioration of the vagal vasoconstriction, whether by cardio-sensory denervation, by the use of drugs, by deep surgical anaesthesia or by active coronary vasodilatation reduces the incidence of sudden death appreciably. The authors suggest the use of full doses of atropine and the drugs causing coronary vasodilatation such as the salts of theobromine and theophylline in large amounts. Atropine is given at least 1/75 grain or better 1/50 grain and the effect continued by 1/150 grain every four or six hours. Aminophyllin is given from 5 to 7½ grains every four to six hours by mouth or the same dose intravenously diluted in 20 cc of saline and given slowly. The authors' conclusions from this important clinical and experimental study are as follows:

- 1 The myocardial infarct responsible for sudden death need not be so large that muscular failure alone is responsible.

- 2 Myocardial infarction may occur without complete closure of a coronary artery and without the classic syndrome of pain, shock and collapse.

- 3 A myocardial infarct usually causes some symptoms, even though they may be mild.

- 4 The sudden death of a patient with infarction of the myocardium is due to a reflex coronary vasoconstriction whose stimulus is the infarct, whose afferent pathway is the cardiosensory innervation and whose efferent pathway is the vagus. The result of this reflex vasoconstriction in a susceptible person is fatal ventricular fibrillation.

- 5 The probability of the establishment of this lethal reflex may be decreased by use of certain drugs (atropine and xanthine derivatives), by cardiosensory denervation and reasonably but to a lesser extent by simple rest in bed.

POTASSIUM THIOCYANATE IN HYPERTENSION

Since Barker's report, in 1936, potassium thiocyanate has been used in the treatment of hypertension in certain cases from the wards and dispensaries of this hospital and the private practices of the authors. Until April 14, 1940, 168 persons had been so treated. Only 101 of these 168 patients have been followed long enough and have been under sufficiently close observation to estimate the results of the medication. In fifty-nine cases the treatment has been successful, and in forty-two, unsuccessful. The treatment was regarded as successful when the patient maintained a systolic blood pressure of 170, or lower, a diastolic of 110, or lower, and felt subjectively improved, while the blood content of thiocyanate was 8 to 11 mg per 100 cc of serum. Failure meant either that the blood pressure did not fall or that the patient felt worse when it did.

The administration of thiocyanate is most likely to be efficacious in the treatment of hypertension if the minute vessel pressure is normal and the capillary count and minute vessel pressure react

normally to histamine. Any variation from the normal response to the various tests which we employed makes success less likely. The treatment is least likely to succeed when an elevated minute vessel pressure is associated with increased cutaneous lymph flow, or when papilledema is present.

—AM HEART JOURNAL, Feb 1941

LANATOSIDE C

Two hundred fifty-six patients with heart disease who have been admitted to the Minneapolis General Hospital since October, 1937, and treated with the recently isolated, crystalline, stable glycoside, lanatoside C (Digilanid C) have exhibited rapid and efficient clinical responses.

The Committee on Nomenclature of the Council on Pharmacy and Chemistry of the A.M.A. recently accepted the terms lanatoside A, lanatoside B, and lanatoside C as scientific (nonproprietary) names for the three cardioactive glycosides isolated from the leaves of *digitalis lanata*. In the early clinical literature lanatoside C is referred to as Digilanid C.

1 Lanatoside C, which is a stable, crystalline glycoside derived from *digitalis lanata*, caused no anatomic changes in the heart muscle of the dog when it was given in therapeutic doses daily for a period of three months.

2 Lanatoside C, when administered intravenously to patients with auricular fibrillation, reduces the heart rate to normal within twenty-four to forty-eight hours.

3 Lanatoside C is efficacious in the treatment of congestive heart failure when normal sinus rhythm is present. In fact, the efficacy of lanatoside C in the presence of normal sinus rhythm is almost as great as when the heart failure is associated with auricular fibrillation.

4 Lanatoside C will often restore normal rhythm in cases of supraventricular paroxysmal tachycardia and auricular flutter. In eight of our 102 cases of nonparoxysmal auricular fibrillation, normal sinus rhythm became established spontaneously during treatment with lanatoside C.

5 Lanatoside C will reduce the pulse rate to normal in some cases of auricular fibrillation associated with hyperthyroidism, and, in at least one case, the venous pressure was brought down from 22 cm of water to 9 cm of water within forty-eight hours.

6 Lanatoside C seems definitely less toxic than preparations of *digitalis purpurea*. Some patients who cannot tolerate *digitalis purpurea* can take lanatoside C in sufficient doses to and in the relief of their heart failure.

—AM HEART JOURNAL, Feb 1941

PRIMARY TUBERCULOSIS IN NURSES AND MEDICAL STUDENTS

"Attention was first drawn to possible dangers of late primary infection by Heimbeck (1928), who found a high incidence of tuberculous disease development in those nurses undergoing training in the general hospital in Oslo who were found to have had a negative tuberculin reaction when admitted to training. These observations are confused by the striking difference in the infection rate of those nurses in question (50 per cent positive) and the general population of Oslo city (85 per cent positive at the age of nine years), a difference leading to the inference that many previously reacting foci had healed, which is extremely unlikely. Since Heimbeck's original observations much attention has been given to the professional hazard run by medical students and nurses whose duty often takes them into contact with open tuberculosis. Most records show that clinical tuberculosis develops more frequently in the tuberculin-negative medical students or nurses (all of whom develop positive tuberculin reactions) during or soon after their clinical training than in those known to harbour a prior infection (Scheel, 1935, Edwards, 1937, Myers et al, 1937, Gee, 1935).

A recent intensive study of this problem in 3,336 students entering Lund University shows that in spite of a moderately high general rate of infection (80 per cent tuberculin-positive at fourteen years) the tuberculous morbidity amongst medical students and nurses (11.3 per cent) was considerably higher than that of other students—1.9 per cent (Hedvall, 1940). A study of the primary lesions (Malmros and Hedvall, 1940) developing during the course of these observations showed that about one-third (47) of those students becoming infected (151) showed some tuberculous change and that these changes were frequently "rather malignant and progressive". Thirty-five of the forty-seven showing evidence of their infection were medical students or probationer nurses. In only fourteen were typical "primary complexes" demonstrated without other lesions. Another fourteen "pulmonary tuberculosis" developed without any evidence of a primary lesion. The value of these statistics for general application is thrown into considerable doubt when it is admitted (Hedvall 1940) that sixteen primary infections were acquired by medical students during a course in general pathology, and before there had been any clinical contact with patients. These were probably owing to infection in the post-mortem room—a hazard peculiar to the institution at the time of the survey, and since rectified.

In spite of the uncertainty caused by these and similar studies, it seems that primary infection acquired under normal conditions, whether in extreme infancy, adolescence, or adult life, is not more malignant than that developing during childhood."

THE PROBLEMS OF PRIMARY TUBERCULOSIS

G M A Hall discusses (Br J Tuberculosis, July-Oct 1941), the problems and paradoxes of primary tuberculosis. The fact that the ordinary course of life in civilised countries results in the infection of a majority of persons before they reach adult life suggests that man is an animal who is extremely susceptible to tuberculosis. That so few of those infected suffer in any way from their infection suggests, paradoxically, that man possesses a high degree of resistance to this disease. All children do not become infected at the same time, when exposed to equal infection from the same source, but few, if any, of them resist for long the repeated infections of a contaminated family environment. Man's natural resistance is not adequate to prevent infection where contact has occurred, nor is this resistance affected by the state of general health. In a certain proportion of cases the development of the well-known Ghon focus marks the site of first infection, and can be demonstrated during life, but in a larger number of individuals the only evidence of infection is the positive reaction to tuberculin.

Primary tuberculosis rarely produces any symptoms or signs of ill-health, even when these are carefully looked for. Occasionally a pleural effusion develops with its classical symptoms and physical signs. This may proceed to empyema and extension, and so lead to serious ill-health and even death. *Epituberculosis* must be considered as a complication of primary tuberculosis. Though occurring in the allergic period, it is now known that the enlargement of the hilum glands related to the primary focus causes collapse of a main bronchus and atelectasis of the corresponding lobe. It runs a benign course and clears without treatment, but may be responsible for the development of bronchiectasis in some children. In some cases a bacteraemia and more or less generalised dissemination of bacilli occurs during or soon after the development of the primary focus. Bacilli entering the venous circulation will be subjected to the filtering action of the pulmonary capillaries, and many of them will again find lodgment in the lungs. Bacilli escaping filtration in the pulmonary circulation will enter the general arterial circulation and so plant the field for the subsequent development of tuberculous lesions in the bones, joints, and other organs.

At one time it was thought that any tuberculous infection occurring in a child under the age of two years was inevitably progressive and fatal. The careful observations and statistics of Miriam Brailey show that this is not the case. Of white children living in a tuberculous environment in Baltimore and showing a positive tuberculin reaction before reaching the age of two years, 87 per cent were still alive and well at the age of five years. Primary tuberculosis may presumably develop in any organ or tissue of the body. Because of their greater exposure, the lungs and the intestines are the most frequently affected. The apices of the lungs are less likely to show the scars of invasion.

than the remainder of the lung field, and the primary nodule is frequently situated immediately beneath the pleura

Though itself a benign condition, primary tuberculosis produces changes in the tissues which set the stage for the malignant and progressive forms of reinfection tuberculosis. Were the immunological changes produced by the first infection of such an order that reinfection of allergic tissue were prevented, tuberculosis would cease to exist as a disease of mankind. But this is not the case, and though reinfection may be resisted, it is not prevented. In this respect, tuberculosis seems to differ from the other great granulomatous disease, syphilis, in which primary infection is invariably progressive and in which reinfection cannot take place while disease, even though it be entirely latent, exists in the body.

The ideal state for the community is that of complete freedom from infection, and efforts to control tuberculosis should be directed towards the eradication of all sources of infection, rather than towards the production of specific immunity. Where, however, infection and the risk of early and repeated reinfection may be expected, some value to the individual may result from an artificially produced infection with non-virulent bacilli, provided time is given for immunity to develop and tissue hypersensitivity to wane before exposure to reinfection is allowed.

The discovery of a primary infection in a child should not condemn it to a life of chronic invalidism, but should lead to the examination of its contacts with the expectation of the discovery of a source of infection, the successful handling of which will protect the child from any consequences of its infection, and possibly save the life and health of many other persons.

COD LIVER OIL AS A LOCAL TREATMENT

Andrew L. Banyal of Muirdale Sanatorium, Wisconsin, U.S.A. describes (*Br Jour Tuberculosis*, July-Oct 1940, pg 107) his experience with Cod liver oil as a local treatment for tuberculous lesions.

Loehr's local use of Cod liver oil in a large number of non-tubercular conditions with success encouraged the author to use Cod liver oil locally in tubercular lesions. Cod liver oil exerts a striking inhibitory effect upon the bacterial flora of wounds and *Streptococci*, *Staphylococci* and *Bacillus Coli* perish when introduced into Cod liver oil. Cod liver oil and tomato juice are used with favourable results in intestinal tuberculosis. Perhaps the Vit A in Cod liver oil and Vit C in tomato juice are in some way responsible for the improvement in the condition of the ulcers. In tubercular pharyngitis and laryngitis the Cod liver oil is sprayed on the throat and the larynx by means of an ordinary atomiser three times a day. Ordinary medicinal Cod liver oil is used. Sterilisation of the oil is not necessary. Most of the cases responded to treatment and the relief from the disagreeable symptoms was prompt. The use of

cocain spray, anaesthesine or euphagin soon became unnecessary. The dryness, tickling, burning sensation and the pain in the larynx or radiating to the ear disappeared after a few days. Cough diminished, the expectoration became easier and the patient's general condition improved. The change in the laryngeal findings were striking. The author has successfully used Cod liver oil in a variety of tubercular conditions such as tubercular ulceration of the tongue, tubercular pleurisy, empyema (45-300 cc of cod liver oil left in the thoracic cavity without any local or general reaction), tubercular fistula, tubercular lymphadenitis, tubercular phlyctenar conjunctivitis, tubercular epididymitis, ischio-rectal fistula and scrofuloderma. The author's conclusions are —

1 A report on the topical application of cod liver oil in 270 cases of tuberculosis is presented

2 Cod liver oil can be used with safety in the conditions described below

3 Pharyngeal and laryngeal ulcers showed a rapid epithelialisation and healing. Favourable therapeutic response was seen in laryngeal tuberculosis with localised infiltration and with a vegetative granulation. Laryngeal tuberculosis with marked oedema is rather resistant to this treatment.

4 Tuberculosis empyema in the absence of bronchopleural fistula responds favourably to aspiration of the pus and to its replacement by cod liver oil. The presence of a bronchopleural fistula does not contraindicate the use of the oil, but the results are much less satisfactory.

5 Suppurating tuberculous lymph nodes, when seen early, heal well on repeated aspirations followed by injection of cod liver oil.

6 The oil when used in the form of eye drops is harmless. It induced more rapid recoveries in our phlyctenular conjunctivitis and keratoconjunctivitis cases than other methods of treatment. The results were unsatisfactory in tuberculous keratitis.

7 Cod liver oil is of some value in treating cold abscess secondary to bone tuberculosis, provided proper attention is paid to the treatment of their source.

8 Fistulas originating from tuberculous epididymitis healed rather promptly on cod liver oil injections. The response in tuberculosis of the urinary bladder was disappointing although there was some improvement in frequency and dysuria.

9 Satisfactory results were observed in the great majority of ischio-rectal fistulas.

10 The results were invariably good in scrofuloderma. Four out of five cases of lupus vulgaris responded favourably to the topical application of cod liver oil.

DIAGNOSIS OF CARCINOMA OF PANCREAS

(E J BERK, ARCH INT MED 68 528, Sept 1941)

A poll among the fourth year medical students, internes, residents and general practitioners of less than five years standing, comprising a group of 120 persons representing 34 medical schools revealed that 43 per cent of the younger or presumably better trained persons considered painless Jaundice as the initial predominant manifestation of the carcinoma of the pancreas. Another 50 per cent stated simple jaundice to be the initial manifestations. Only 2.5 per cent of the persons polled considered abdominal pain to be of primary importance.

Analysis of the data of 35 proved cases of carcinoma of the pancreas admitted to the Graduate hospital of the University of Pennsylvania considered along with similar analysis from other authors showed that epigastric pain figured in over 50 per cent of the cases as the initial symptom. Contrary to the prevailing impression abdominal pain as an initial symptom comes in frequency next only to loss of weight which was present in 90.1% of the cases in the authors' series at the time of admission into the service. Next in the order of frequency were noticed nausea, vomiting and anorexia.

In summing up the differential diagnosis the author considers radiographic evidence valuable as one or the other of the following changes were noticed in over half the number of cases:

(1) Obstruction at some part of the duodenum usually in the third part or at the pylorus with stenosis in the proximal part (2) Irregularity and deformity of the pylorus and duodenum from infiltration and encroachment and (3) Widening of the sweep of the duodenum.

A plea for early diagnosis is made as the average duration of life after the onset of symptoms was six months. Some of the newer laboratory aids as estimation of serum lipase and amylase may be valuable adjuncts in the diagnosis.

P RAGHAVAN

CARCINOMA HEAD OF PANCREAS

S C Franco, (Amer Jour of Diges Dis, VIII, March 1941) analyses the data obtained from 40 proved cases of carcinoma of head of pancreas from the Long Island college hospital. Fourteen of these were proved at autopsy and the remainder at operation. Only one arose from the ampulla of Vater, one from the lower bile ducts and the rest from the head of the pancreas. Over 50% of the cases occurred in the sixth decade or beyond. The symptomatology, laboratory and radiographic findings are discussed. The average duration of life between onset of symptoms and death in his series was two and a half months. It is pointed out by the author that carcinoma head of the pancreas should be considered in the

differential diagnosis when there is a suspicion of malignancy but the gastro-intestinal radiographic picture is negative or dubious

P RAGHAVAN

EFFECT OF FEEDING APPLE SAUCE ON INDUCED DIARRHOEA IN RATS

Z I Kertesz, M S Walker, Z C M McCay (Amer Jour of Dig dis VIII 124 April, 1941), conducted the following series of experiments to determine the efficacy of a commercial apple sauce preparation in curing diarrhoea and secondly the particular fraction of the apple sauce responsible for the cure. They induced diarrhoea in rats 3 weeks old (corresponding to children two years of age) by feeding them on lactose and milk. To one batch of diarrhoea rats they fed apple sauce, and found its co-efficient of efficacy to be 84%. When a preparation from the apple sauce, in which the pectins were completely destroyed by pectinase, was given to another batch of diarrhoeic rats, it was found to be effective by only 39%. To a third batch they gave pure pectin, obtained from the same apple sauce, by successive hot water extractions and precipitation by alcohol and subsequent concentration. It was found to be effective by only 23%, contrary to expectations raised from the results of the first and second series of experiments. The authors explain this discrepancy as being due to difference in the water content of the sample of pectin. To a fourth series of diarrhoeic rats they gave the residue left after extraction of pectin, and it was found to be effective by 53 per cent.

From these experiments they conclude that in the present series of experiments at least the anti-diarrhoeic action of apple sauce depended upon pectin and crude fiber content of the material, both of the constituents acting in virtue of their colloidal and adsorbant properties.

P RAGHAVAN

PECTINS IN DIARRHOEAS

S C Welch & H C Ivy Fate of ingested pectin (Amer Jour of Diges, diseases VIII 101 April 1941)

Vegetable Pectins are being used in the treatment of diarrhoeas particularly for non specific diarrhoeas of infants. Its mode of action as well as the fate of ingested pectin are as yet unsolved problems. It has been held that pectins act by absorbing toxic substances. If the pectins get decomposed in the intestine the above contention would be untenable. It has been held by others that pectins are split into galacturonic acid which is absorbed and performs a detoxicating role in the liver by forming uronates and phenolic substances. If however it could be demonstrated that pectin is not split into galacturonic acid in the intestine or that the galacturonic or uronic acids produced in the intestine are absorbed. The second view

becomes untenable. The authors undertook to perform a series of experiments to determine the co-efficient of digestibility of the pectins.

Two dogs were fed on 20 grms of pure citrus pectin daily along with a diet of low crude fiber content, after having been on a period of basal diet alone. The pectic acid, pectin uronic acid contents of the faeces analyzed. It was found that no pectic acid could be obtained during the period of basal diet alone. During the second period as much as 90 per cent of the ingested pectin disappeared. When subsequently the same dogs were fed on pectin alone during starvation it was found that only 50 per cent of the ingested amount was decomposed. In two dogs which defecated more frequently during starvation, 70 per cent to 90 per cent of the ingested pectin could be recovered. The results obtained in the normal human beings who were given 50 grms of pectin with a basal diet of low crude fibre content the result was essentially same for 90 per cent of the ingested pectin was decomposed in the intestine. However, during fasting human beings were able to utilise more pectin than dogs.

Experiments were also conducted on two dogs on whom ileostomy was performed and two human beings on whom similar operation had been performed for chronic ulcerative colitis, and the material obtained after giving pectin to these subjects was analysed for pectin content. In dogs 84 per cent to 89 per cent and human beings 94 to 97 per cent was recovered in a 'twenty-four hours' study while in a twelve hours' study on human being the amount recovered ranged from 72% to 80% of the quantity ingested. The human beings complained of flatulence while being on pectin.

From the results obtained it was concluded that both dogs and human beings decompose the greater part of the ingested pectin and that the breakdown occurs mainly in the colon and not in the upper intestine. Bacterial enzymes rather than digestive juices seem to be involved in the breakdown.

P. RAGHAVAN

MOLLUSCUM CONTAGIOSUM

James Sommeville (Brit Jour of Derm & Syph Aug & Sept 1941), reports an interesting experiment in a case of Molluscum Contagiosum with severe secondary infection. Hesitating to use the customary local treatment on account of the secondary infection he used M & B 693 to allay the latter. The case was an extensive one with 75 lesions noted. After a week on the drug the secondary infection had completely subsided and with it the lesions of Molluscum Contagiosum had also gone down. This encouraged a further trial with the drug on a reduced scale, and after a week further retrogression of the lesions resulted, curtailing the drug still further for another week caused complete subsidence in the lesions, leaving a few temporary scars. The patient had received in all 49 Grms of

M & B 693 in four weeks. As the drug has been found useful in Lymphogranuloma Inguinale which is also due to a virus, he determined to try it out in other cases of Molluscum Contagiosum. A girl of 13 with the lesions was given 98 tablets in five weeks to effect a cure. A boy of 16 was given irregular treatment for 8 weeks and cleared up entirely. Another boy of 13 was also treated irregularly and cleared in 9 weeks. An infant of nine months who was put on half a tablet four times a day for two months, off and on, without improvement responded to a dose of one tablet four times a day, after seven days of further treatment. A girl aged five responded in two weeks to one tablet four times a day.

The author concludes that M & B 693 has a definite lethal effect on the virus of Molluscum Contagiosum. Fairly high dosage must be given and may have to be protracted over some weeks—two weeks being the least in his experience. He states that he does not mention this as a new treatment for the disease which can so easily be treated by local applications, but as an interesting experiment to a member of the virus group of infections.

I. HERNANDEZ

GONORRHEAL URETHRITIS

Uhle Latowsky and Knight (JAMA Volume 117 No 4) give the results of a study of Gonorrhoea treated with Sulphapyridine and Sulphathiazole in two parallel groups of cases comprising 87 and 55 patients respectively. All the patients were given ambulatory treatment and all were males. They express their opinion that it is preferable to use standard routine treatment along with Chemotherapy but in this series of cases, it was decided to limit the treatment of every patient to oral, owing to the large number of patients seen within a short space of time. In the first group of 87 cases treated with Sulphapyridine, 62 were followed up, 25 defaulted, 57 or 92% were cured, 5 or 8% were not cured. A further analysis shows that of the 62 cases, 43 had acute anterior urethritis and 16 acute posterior urethritis, and 3 cases had sub-acute urethritis. Of the 55 cases treated with Sulphathiazole, 5 defaulted, 48 or 96% were cured and 2 or 4% were not cured. Of these cases, 31 had acute anterior urethritis, and 17 acute posterior urethritis, and 2 had sub-acute urethritis. The failures were due to resistant strains of gonococci on which small or large doses did not react, or to failure of co-operation on the part of the patient.

The authors do not claim an immediate cure e.g. the 92% in the Sulphapyridine treated group represents an average of 51 days, with a range of from 14 to 162 days for a cure to be effected. In comparison 96%, in the Sulphathiazole treated group represents an average of 28 days with a range of from 7 to 28 days for a cure. These figures represent the time elapsing from the time the drug was begun to the appearance of the first negative culture for gonococci. The average duration of discharge, in the Sulphapy-

ridine group was 3 days with a range of from 2 to 8 days, and with Sulphathiazole, 3 days with a range from 1 to 7 days. It is to be noted that the clinical response is much more rapid than that obtained with local therapy alone and secondly the complications are reduced or actually prevented. In the whole group of cases cured no complications were reported.

The average dosage of both the drugs to effect cure was 3 gm. It was found that to produce a cure with Sulphapyridine, the dosage ranged from 2 Gm daily for 7 days (14 Gm) to 3 Gm daily for 37 days (111 Gm), and for Sulphathiazole, from 3 Gm daily for 4 days (12 Gm) to 3 Gm daily for 28 days (84 Gm). The drugs have in some cases to be given for more than 8 to 10 days which is the safe limit. The authors therefore advise that it would be better, to avoid toxic symptoms, to give the drugs in two courses of 10 days each with a brief interval in between, in those cases where it is necessary.

Three patients of the 87 treated with Sulphapyridine over a prolonged period developed exfoliative dermatitis.

It is customary to give smaller doses to ambulatory patients for obvious reasons. From among 76 of the Sulphapyridine treated patients reporting during the treatment 75% experienced mild toxic symptoms. Among 52 treated with Sulphathiazole 11.5% experienced mild symptoms.

The authors express the view that Chemotherapy has destroyed the value of provocative tests as the patient has gone into a clinically negative phase and will not respond to the routine of provocation even though smears and cultures may be positive. Most reliability should be placed in smears and cultures. The authors stress the greater reliability of the cultures over the smear, and contend that three sterile cultures obtained at intervals of 5 to 7 days should be taken as evidence of cure. The importance of recognising the carrier state is very great. The early disappearance of symptoms giving a false sense of security to the patient who may transmit the disease to others, without apparent harm to himself, and therefore also risk a chance of reinfection, at a later date from his sexual partner. The carrier state in this series for Sulphapyridine ranged from 2 to 50 days and for Sulphathiazole from 3 to 53 days.

J FERNANDEZ

TREATMENT OF INTESTINAL PARASITES

Ernest Faust recommends the following chemotherapy for intestinal parasites (J.A.M.A., Oct 1941)

(a) *Amoebiasis*. He stresses the point that all cases of amoebiasis, whether symptomatic or asymptomatic must be treated till cured. There is no single drug which will completely eradicate amoebic infection. Hence the treatment is preferably combined

i Emetine is useful mainly in acute cases

ii Chinofon (iodoxyquinoline sulphonic acid) is the drug of choice

- iii Entero-vioform (Iodoxyquinoline and supanone) needs further clinical trials (In our opinion Entero-vioform is effective in both acute and chronic amoebiasis. It can also be administered per rectum as a retention enema)
- iv Carbarsone is the chief arsenical preparation to supplement the treatment

(Note We would like to add that preparations of Kurchi, which are easily available in India, should be given extensive trials) -

(b) *Giardiasis* Atabrine is apparently specific

(c) *Oxyuriasis* (Thread-worms—Gentian Violet is the drug of choice. The dose for an adult is one grain thrice daily for one week, followed by an interval of one week, and then followed by another course for a week

(d) *Ascariasis* (Roundworms) He recommends Caprokol (Hexylresorcinol crystals) in hard gelatin capsule in a single dose of grains 10 to 15. He says it is non-toxic and is more effective than santonin. The usual routine of a saline purgative preceeding and following the drugs is followed

(e) *Hook-worms* Tetrachlorethylene is the drug of high efficiency and low toxicity. Caprokol is next best

(f) *Tape-worms* Oleoresin of aspidium in a total dose of 60 minims, administered in three doses of 20 minims each, is best. Carbon Tetrachloride is the next best substitute

(Note *Giardia lamblia* are commonly found in stools of patients in Bombay. Regarding *Giardiasis* it is not decided whether *Giardia lamblia* causes any pathogenic lesions in man. Some deny it. But Haitman and Kyser in a recent article quote material to suggest that it causes inflammatory changes in the gastro-intestinal and the biliary tracts, sometimes producing severe symptoms. In view of the present knowledge all cases of *Giardiasis* may be treated with Atabrine or its equivalents e.g. Quinacrine, Crinodora etc. The dose is 1 tablet (0.1 gm) three times a day for five days)

MJS

TREATMENT OF MALARIA

Coggeshall, Maier and Best, (JAMA Sept 27, 1941) suggest that though quinine and atabrine are very effective to control an acute attack of malaria, they cannot eradicate the infection completely. Hence it is necessary to search for better anti-malarial drugs. As a result of their studies on experimental malaria and human malaria, they show evidence that (1) Promin (N,N-didextrose sulphonate) and (2) Sulphadiazine (2-sulphanilamide pyrimidine) possess considerable anti-malarial activity

(Note These drugs are allied to Sulphanilamide and the observation that they are still in a state of trial. Quinine and Atabrine are still to be used for malaria)

MJS

SULPHADIAZINE

A new chemotherapeutic agent The search for an ideal chemotherapeutic drug, showing maximum effect with no toxic side effects continues Sulphadiazine has been tried by Finland, Strauss and Peterson in 446 patients suffering from various infective conditions caused by Pneumococci, Staphylococci, Streptococci, Meningococci, B. Coli, and Gonococci They report the drug to be as effective as Sulphapyridine and Sulphathiazole and to be less toxic

Dingle, Thoman and Morton report 13 cases of Meningococcal meningitis with 1 death (which occurred with 10 hours of treatment) and with complete recovery in others

(Note Sulphadiazine seems to be more promising from the present reports But, until further extensive trials are reported, the drug should be considered to be in an experimental stage)

M J S

The Clinical Toxic Manifestations of Sulfanilamide, Sulfapyridine and Sulfathiazole with the Time of Their Appearance in the Course of Therapy

Toxic Manifestations	Sulfanilamide	Sulfapyridine	Sulfathiazole
Nausea and vomiting	Uncommon occurs early	Very frequent occurs early	Rare
Dizziness	Common occurs early	Common occurs early	Uncommon
Cyanosis	Very common occurs early	Faint common occurs early	Uncommon occurs early
Acidosis	Common if so hemolytic anemia is not given occurs at any time	Not reported	Not reported as yet
Mild hemolytic anemia	Very common early and late	Common early and late	Not reported as yet
Visual disturbances	Rare	Rare	Not reported as yet
Gastrointestinal tract	Bleeding rare diarrhoea uncommon	Bleeding reported	Not reported

Best to stop drug and force fluids

Psychoses	Rare occur early	Not reported	Not reported as yet
Neuritis	Rare generally early	Not reported	Not reported as yet
Fever	Common generally 7th to 9th day may occur from 1st to 21st day	Uncommon generally early 5th to 9th day may occur from 1st to 21st day	Common 5th to 9th day
Rash	Common may take almost any form generally 5th to 9th day may occur 1st to 21st day	Not very common generally 5th to 9th day may occur 1st to 10th day	Very common generally 5th to 9th day
Hematuria	Not reported	Common 1st to 10th day	Common 1st to 10th day
Hyperleucocytosis	In presence of acute hemolytic anemia	In presence of acute hemolytic anemia	Not reported as yet
Acute hemolytic anaemia	Common especially in Negroes generally 1st to 5th day	Uncommon generally early 5th day	Reported as occurring
Injection of sclera and conjunctiva	Not reported	Not reported	Common especially in conjunction with rash and fever 5th to 9th day
Painful joints	Reported	Not reported	Reported with rash
Stomatitis	Rare	Not reported	Not reported

Imperative to stop drug and force fluids

Hepatitis	Rare early or late	Rare early or late	Not reported as yet
Anuria with azotemia	Not reported	Not uncommon 2nd to 14th day blood pressure and fundi normal	Not uncommon
Acute leucopenia with granulocytopenia	Not common 1st to 10th day	Common especially in children 1st to 10th day	Not common 1st to 10th day
Agglutocytic anemia	Uncommon generally between 17th to 25th day may occur 14th to 10th day	Uncommon generally between 17th and 25th day may occur 14 to 10th day	Not reported as yet
Purpura hemorrhagica	Rare	Rare	Not reported as yet
Jaundice	With hepatitis or acute hemolytic anaemia	Rare	Not reported as yet

Book Reviews and Notices

ELECTROCARDIOGRAPHY By Louis N Katz, Lea and Febiger, Philadelphia, 1941 pp 580 Rs 37-8-0

There has been an increasing need felt of late in medical circles for a book of this kind on electrocardiography. The author can certainly be complimented on the massive information he presents to the busy practitioner within the space of a few hundred pages and more so for the excellent choice of illustrative material presented throughout with a view to facilitate the understanding of the subject of electrocardiography.

There is no doubt that this book will bring to its author the appreciation and thanks of many a practitioner and specialist, who has interest in this subject. The primary object of the author in presenting this volume to the clinician, viz "to acquaint the reader with the several aspects of the field of electrocardiography", has, in our opinion, been amply fulfilled. After a perusal of this volume, one can well succeed in interpreting even difficult electrocardiograms, rationally and systematically.

The author has conveniently considered his subject in three parts, each self-contained and complete. In the first section, comprising of 4 chapters, the author deals with the theoretical aspects of electrocardiography, a knowledge of which is so essential for a proper understanding of the subject.

In the second section, the author presents a systematic and exhaustive account of various electrocardiographic patterns met with in practice, both under physiological and under pathological conditions. There is a description of the normal electrocardiogram at different ages of life. Chapter VIII, which deals with the electrocardiogram of coronary disease is perhaps the most important chapter of the book. Departing from the conventional method of describing coronary disorder, Katz classifies Coronary insufficiency into distinct groups, depending on the rate at which events proceed (1) Transitory coronary insufficiency (2) Acute fatal coronary insufficiency (3) Protracted coronary insufficiency which presents itself clinically as the classical syndrome of myocardial infarction. One cannot but envy the author his excellent collection of electrocardiographic records of coronary cases.

The third section of the book is devoted to a consideration of the various arrhythmias of the heart, which have conveniently been classified into two groups viz Disturbances of Impulse Initiation and Disturbances of Impulse Conduction.

In spite of the fact that this book has not been designed by the author as a book of reference, the bibliography presents almost a thousand references of topical interest. Besides, including a certain number of references of historical interest, it contains a large

number of modern contributions from American and European authors. Anyone who wishes to have a working knowledge of this all-absorbing science is recommended this book as a veritable source of information and guidance. It is destined to go down in medical history as a classic.

R J VAKIL

THE HEART SOUNDS IN NORMAL AND PATHOLOGICAL CONDITIONS By Oscar Orias and Braun-Menendez Oxford University Press London 1939 pp 258 Sh 15/-

One cannot help but congratulate these two authors on having added to modern medical literature an excellent new monograph on an absorbing subject like that of heart-sounds. Though Hippocrates, the father of medicine is said to have been familiar with heart-sounds, the first real reference to them we owe to Harvey, who described them in 1628. Harvey's work was sarcastically referred to by Paracelsus in 1663 when he made the following "stinging" remark: "nor we, poor deafs, nor any other doctor in Venice can hear them, but happy is he who can hear them in London." This remark will remain in history as a "shameful testament of human stupidity."

The first few chapters of this new book are devoted to physical and physiological principles of heart-sound production and to various methods available for the auscultation or graphic registration of heart sounds. By the graphic recording of heart-sound vibrations (Phonocardiography), a more objective and quantitative analysis of heart-sounds than permitted by auscultation, has been made available to the clinician. Two main groups of phonocardiographic methods are discussed viz direct methods and indirect or electrical methods.

In the second part of their monograph, Orias and Braun-Menendez give a detailed account of the heart-sounds under normal or physiological conditions. Each sound is discussed in detail, historical references to each sound are cited, aetiological theories discussed, and a detailed account given of the graphical configuration of each sound together with records and diagrams.

The authors have demonstrated convincingly, that at least four factors are concerned in the production of the first sound viz (1) the muscular component, (2) the valvular component, (3) the vascular component and (4) the auricular component. A study of the graphic configuration of this sound reveals four distinct groups of vibrations, each of which has been discussed by the authors.

The second sound is much simpler than the first, from the point of view of causation as well as of graphic registration. Their phonocardiographic study serves not only to reveal the complex nature of each heart-sound but also to direct attention to the presence of four and not two (as is commonly believed) normal heart-sounds.

The third part of the book is devoted to modifications in the graphic configuration of heart-sounds produced by various pathological conditions

Gallop rhythm has been classified into 3 main types (a) Presystolic or auricular gallop, where the extra sound coincides with presystole or auricular systole (b) Rapid filling gallop, when the sound coincides with the end of the ventricular filling phase and (c) Complete or incomplete summation gallop. In order to arrive at a decision about the type of gallop in any given case, a simultaneous record of the heart-sounds (phonocardiogram) and the venous pulse (phlebogram) is essential

Evidence is amassed to show that the important auscultatory sign of mitral stenosis known as "opening snap of the mitral valve" originates at the structurally deformed mitral valves and coincides with the opening of the auriculoventricular valves

The application of this new science of phonocardiography to the analysis of murmurs has proved disappointing in the opinion of these authors

We have no hesitation in commending this book to all students and practitioners who are the least bit interested in the graphic recording of physiological phenomena, phonocardiography will serve to unravel mysteries which have so far remained impregnable to the cruder methods of auscultation

R J VAKIL

REGIONAL DIAGNOSIS IN LESIONS OF THE BRAIN AND SPINAL CORD By Robert Bing Translated and Edited by Webb Haymaker, St Louis, 1940

When a small book of less than 300 pages goes into print for the eleventh time and is accorded the honour of being translated into another language, it stands to reason that such a book must possess some outstanding quality. Such a book is Bing's treatise on the subject of neurological localization, a book that has had "excellence and vitality to remain for thirty years an outstanding authority" on the subject it portrays

The most commendable feature of this book is that it is essentially "practical" or applicable to clinical practice, realizing the futility of a merely theoretical approach, the author has tried to avoid too many theoretical or hypothetical discussions and prefers to stick to recorded observations. Within the short compass of just over 200 pages, the author has succeeded in amassing a lot of data regarding localization of brain and spinal cord lesions, in a systematic and orderly manner. The first part of this book is devoted to spinal cord lesions and the second part of cerebral lesions

According to Eng, when confronted with a lesion of the spinal cord, there are two aspects of localization to consider, (1) to determine the site of the lesion in the *transverse* plane i.e. whether it is right-sided or left-sided, anterior or posterior, central or peripheral, and (2) to determine the site of the lesion in the longitudinal plane i.e. the exact level or segment of the lesion. For this purpose a detailed knowledge of anatomy is essential.

After reviewing the anatomy and physiology of the various conduction systems of the spinal cord in the first two chapters, the author discusses the problem of localization from the point of view of signs, symptoms and syndromes. There follows a brief reference to certain "syndromes" or 'symptom complexes" which facilitate the problem of localization.

The second part of the book begins with an account of the morphology of the "brain-stem" (which includes the medulla oblongata, pons and the mesencephalon). Sections are described at various levels of the brainstem. The importance of involvement of cranial nerves and their nuclei is discussed. Chapters on the localization of lesions causing speech and visual disturbances are particularly instructive.

From cover to cover, this beautifully illustrated book will afford a wealth of information to the busy diagnostician. To the student, not so conversant with neurology, it will present a concise introduction to the principles of localization of Diseases of the nervous system. A neurological classic, it will do justice to any library.

R. J. VAKIL

The Indian Physician

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LIVERGEN

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Indigenous drugs —

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 Psychotria seed Tenuppleek,
 Hygrophilla spinosa
 Oldenlandia corymbosa,
 Curum Roxburg. hianum

B P Drugs —

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Let us remember...

CHARLES RICHEL

(1850-1935)

ON THE GENESIS OF EXPERIMENTS

(CHARLES RICHEL, Professor of Physiology in the University of Paris for many years and a Doyen of the Medical Faculty, is familiar to all medical men as an eminent worker in physiological and pathological sciences. He was well known to be a man of letters as well as a man of science. In 1923, he wrote a humorous book called *Le Savant*, and presented it to the Academie des Sciences. Sir Oliver Lodge translated it in English, under the name of *The Natural History of a Savant* (J M Dent & Sons, Ltd, London). The book contains an autobiographical chapter,—“ON THE GENESIS OF EXPERIMENTS”—which gives some insight into the method of work of the eminent scientist. How do scientists work? How do they plan their experiments? Many literary writers, novelists and poets, have written about their methods of work but few scientific workers have left such intimate confessions. Charles Richet's personal account of his method of work may be read even today with interest and perhaps inspiration by all scientific workers.)

Once again I am going to ask pardon of my reader, since I am going to talk about myself. But it will be in all modesty. Indeed, I want to show how, in any discovery, whether slight or important, our personal role counts for very little, so little that it amounts to nothing. It will be a rather humiliating profession of faith, since I attribute a considerable role to chance. Nevertheless, it will be recognized that chance was aided by perseverance.

I think that this naive confession will be useful to young people, for we shall witness the genesis of a piece of work, and realize the phases through which the experimenter, guided by the facts themselves rather than by his own ideas, at last

succeeds in establishing some new phenomenon which had previously passed un-noticed

I

My researches on gastric juice may be said to have been due to chance, but to chance fertilized by three masters

My loved master Verneuil, whose pupil I was at that time, had performed a gastrotomy operation on a boy whose oesophagus had been obliterated by the accidental swallowing of caustic potash in solution. This bold operation then quite new had succeeded, so that this young Marcelin had a fistula left into his stomach, through which the gastric juice drained and by which one could introduce food, for his oesophagus was completely gone. Verneuil said to me "Repeat on Marcelin the admirable observations of Beaumont on his Canadian, and you will be sure to find interesting things." So, in Berthelot's laboratory, I began to study the gastric juice of Marcelin. I even noted, in passing, a fact which unfortunately I scarcely spoke of and on which I did not insist as I ought, a fact which was so well brought to light by Pawlow, namely that mastication and swallowing of food provoke by psychical reflex the efflux of gastric juice. It was truly remiss of me not to study this phenomenon more closely, I ought then and there to have demonstrated this gastropsychic secretion, which Pawlow, twenty years later, analysed with so much penetration. I tested the acidity of the gastric juice, before, during, and after digestion, when one day Berthelot said to me "Try what you can get by the method of fractional separation (proportional solubility of the acids in water and in ether), you would be able thus to settle the controversial question of the acidity of the gastric juice,"—which was done, not without notable difficulties over which I must not delay. I have already recounted how Claude Bernard, meeting me in the court of the College de France, said to me "Study the gastric juice of fishes, it is of extraordinary activity"

Did I not do well to follow the advice of my illustrious chiefs, Verneuil, Claude Bernard, Berthelot? We can never have sufficient gratitude for the suggestions given us by eminent masters

II

It was chance also that led me to ascertain the nature of la polypnee thermique (panting from heat). No theory urged me

to it I set out with an idea which appeared to have no bearing on the question But—and I think that this is commendable—when facts present themselves to me, I am not obstinate in my opinions, I adapt my ideas to the facts which I observe

There is a classic line which I wish to reverse

Et mihi res non me rebus subjungere conor

This precept seems to me to advocate a tactical error (at least as regards scientific procedure) I try to submit myself to facts, without any foolish attempt to make them submit to me

I will describe by what unexpected detours I came to understand how dogs cool themselves by breathing rapidly It is now a phenomenon so simple, so classic, so evident, that it is difficult to believe that it had not been always known But no! certainly not! Before my memoir of 1885, the word "polypnee"—which I invented—did not exist, and no physiologist had understood the cause and the mechanism of this thermic polypnoea, which was confused with dyspnoea (difficult or obstructed breathing), and nobody understood its significance

It was by successive stages that I arrived at this notion, and very indirectly I knew, as do all physiologists, that muscular contraction is due to the combustion of sugar in the blood, so I asked myself whether, by choosing animals in a state of fasting, and tetanizing all their muscles, I could cause their temperature to rise as rapidly as with normal well-nourished dogs I found that dogs electrified and tetanized get just as heated when they are in a state of fasting as when their digestive processes are fully active My hypothesis, therefore, was not justified Nevertheless, I thought I remarked certain difference in the heating of the dogs in which I provoked electric tetanus It seemed to me that muzzled dogs got overheated more quickly than others, and soon became fatally over-heated, whilst unmuzzled dogs, who were able to pant, got very little heated at all A series of experiments, easy enough to devise, permitted me to prove that frequent respiration cools the blood by exhalation of water Thus the cause and the mechanism of thermic polypnoea were established

Very rarely does one succeed in verifying hypothesis formed before beginning a series of experiments Claude Bernard relates that he had supposed, since the sympathetic nerve governs

the functions of nutrition, that in exciting this nerve electrically one would develop heat. But experiment gave him a result absolutely opposite to that which he thought he would obtain by the excitation of the sympathetic, the temperature went down instead of up. This erroneous induction was, however, the point of departure of an admirable discovery, that of vaso-motors. Claude Bernard was wise enough not to persist in his hypothesis, but to adapt himself to the facts, *se subjungere rebus*. Throughout the whole of his glorious life he remained faithful to the teaching of Magendie, his illustrious master. Magendie was delighted when experiment gave result contrary to what he was expecting. "Well!" he used to say, "I was mistaken, but it is much more interesting than if I had succeeded. I foresaw, as probable, a logical orthodox fact, which everybody might expect, and it is just the contrary that happens. There is therefore a new phenomenon, so much the more important as it was so little expected." And Magendie did not hide his satisfaction at having run aground.

III

Once it happened to me that I made a hypothesis that was verified, and I saw my hypothesis and my experiment, amplified by clever physiologists and great doctors, undergo considerable development. It was that of serum therapy, one of the principal conquests of modern therapeutics. So I may be permitted to lay stress on it. For I truly believe that the genesis of a discovery constitutes the most curious part of its history.

Our great physiologist Chauveau had shown that French sheep die from anthrax (*Bacillus anthracis*) when they are inoculated with anthrax blood, but that Algerian sheep, after being infected by the same blood, do not die. Why this difference? In my course of physiology, in 1883, as I was talking of the little-known extractive substances of the blood, I suggested that it might be one of these extractive substances, still mysterious, existing in the blood of Algerian sheep, which opposed the growth of the anthrax bacilli. "Who knows," I used to say, "whether by injecting the blood of an Algerian sheep into a French sheep immunity against anthrax will not be conferred upon the latter?" I advised my students and my assistants to try the experiment.

- We had no sheep in our laboratories, so that for five years my projected experiment remained in the nascent stage. And it was by an absolutely different path that I returned to it.

Among the dogs which were brought to the laboratory, there was found one which had a cancerous unopened tumour. The question was then being asked, as it is still being asked today, whether microbes were not the cause of cancer, so with my friend Héricourt I tried to find some microbe in this cancer, and indeed we managed to isolate one and cultivate it. Naturally, we injected it, hoping to reproduce the same cancer in other dogs, but the failure was complete. It certainly developed a tumour, but only a sort of abscess, which sometimes was reabsorbed and sometimes became purulent. With rabbits, this injected microbe produced a great oedematous tumour, and the animal died in three or four days. On the other hand, dogs, although ill for some days, did not die. And then I thought of using this microbe, mortal for the rabbit, not mortal for the dog, and making the experiment which I had spoken of in my course, five years previously. *"Since the dog is immune by injecting the dog's blood into rabbits, will not they also be rendered immune?"*

At first we encountered a sinister check, for rabbits, after a venous injection, could not stand the dog's blood. At this period (i.e. in 1886) no one had thought of serum, neither myself nor other physiologists. It was the complete blood that we then injected, and all our rabbits died as soon as a few drops had been introduced. Then I thought of overcoming the difficulty by injecting the dog's blood not into the veins, but into the peritoneum of the rabbit. After this peritoneal transfusion, even when abundant, the rabbit did not die. Well, it turned out that the rabbits which had received the dog's blood in the peritoneum resisted our microbe much longer than normal rabbits.

We soon discovered another fact, of extreme importance. When we injected the blood of a normal dog, the rabbit ended by dying of microbial infection, but when we injected the blood of a dog infected by our microbe and cured, the microbe had no longer any hold on the rabbit so transfused, and it survived.

Consequently, by injecting blood, one communicates to the injected animal the immunities possessed by the animal whose blood is injected. That is the whole principle of serum therapy.

And immediately we grasped the vast consequences of the discovery. Then we committed an error, a lamentable error, doubtless very excusable, but an error none the less.

Hericourt and myself, after the rigorous statement of the fact (immunity by blood of immune animals), dreamed of applying it to a disease other than this very special infection of the rabbit. And I remember yet, as if it had been yesterday, the long conversation—for us historic—that we then had. To what malady must we apply hematotherapy—it was not yet called serum therapy—diphtheria, anthrax, or tuberculosis? There were arguments for and against each. Considering the state of science in 1887, and the absolute novelty of the hematotherapeutic method, we had no serious motive for choosing diphtheria rather than tuberculosis, or tuberculosis rather than diphtheria. We decided on tuberculosis.

And this choice was unfortunate, for the serum therapy of tuberculosis is doubtful, whilst the serum therapy of diphtheria gives marvellous results, as, two years later, Behring showed in an admirable piece of work.

So one must admit the part played by chance in scientific things, as in everything else of this world, and I ask myself again by what divination we could have been expected to foresee that serum therapy would cure diphtheria, while tuberculosis it would not cure?

IV

It was chance alone that permitted Hericourt and myself to discover zomotherapie (raw meat treatment), that is to say, the treatment of tuberculosis by the ingestion of the juice of raw meat. Our perspicacity had no great share in it.

Our studies on the serum therapy of tuberculosis went on endlessly. We attempted various treatments for experimental tuberculosis, various vaccinations, various diets, and we devoted ten years to our studies. They were sterile, I am not at all afraid to admit that. Neither creosote, nor arsenic, nor iodine, nor uric acid, nor dieting would give results, no more than would vaccinations with various tuberculous or weakened microbes. But, one day, after having arranged our experimental programme so that there were three dogs for each special treatment, it was found that we had a dog too many, sixteen instead of fifteen.

Then, not knowing what to do with this sixteenth dog, I conceived the idea of feeding it on raw meat

At the end of a month and a half, the fifteen dogs were dead all without exception. The sixteenth alone had survived, this was the dog nourished on raw meat. I thought then that we had made a mistake and that it had not been inoculated with the tuberculosis virus. But no! we could see that it had on its paw the little scar, proof of the injection.

Happily, I recommenced the experiment. But it was I admit—without great conviction, for our blindness is such that unforeseen facts *have to force our hands* to make themselves accepted. And soon it was demonstrated to us that tubercular dogs nourished otherwise than on raw meat succumbed, whilst those nourished on raw meat resisted. Not only did they resist, but they retained robustness, vigour, marvellous health.

Then, but after the event, I understood. I ought to have foreseen it. But neither I, nor anyone, had dreamt of it, until the moment when experiment, far superior to our poor imagination, began to speak so as to make us understand. In all Nature no living things are nourished on cooked foods. Cooked meat, therefore, is not a natural food. Hence this feeding, being in a sort of way abnormal, may not be the best. And the reason for that is easily understood, since the albumens which constitute raw meat are easily transformable into living muscle, whereas that transformation is not so easy if they have been broken up by heat. Therefore, by feeding dogs on raw meat, one is returning to the natural food, and giving them sufficient strength to resist tuberculosis. But this very proper reasoning, childish in its simplicity, we only arrived at *after* experiment, and I recognize the fact in all humility.

The efficacy of raw meat having been once established, the experiments still to be made were all indicated. They were not very difficult. By a few decisive examples we could prove that the juice of meat was the therapeutically active part of muscular flesh.

V

The history of anaphylaxy which has had such good fortune, is another excellent example for showing how much more fruit-

ful experiment is than speculation. Never would I have supposed anaphylaxy possible. Even when it presented itself to us, my dear friend P. Portier, with whom I was working, showed himself entirely rebellious about it. It was *in spite of myself* that I managed to discover *l'anaphylaxie* (the converse of immunity, hypersensitivity to specific disease).

Here are the facts. On the yacht of Prince Albert of Monaco, P. Portier and myself, following the advice of the Prince and Dr. Richard, made some experiments on the Physalidae, Ctenophora of tropical seas, whose tentacles are venomous. And as there were no Physalidae in our climate, but only Actinia, which are very common on all our coasts and which in certain respects resemble Physalidae, I had Actinia brought and from them extracted a poison of which I studied the effects. It was necessary to find the toxic dose, let us call it 1, so that dogs which had received less than 1 should survive after some days of sickness. For convenience I kept them in the laboratory in order to give them another injection later, for, at the end of three or four weeks, they were absolutely cured.

And then appeared an extraordinary fact, now banal enough, which at first I had enormous difficulty in believing. On these cured dogs the feeble dose of 0.1 became immediately fatal. To make sure there was no mistake, I repeated the critical experiment (*experimentum crucis*) on a great fine vigorous dog, injected a month previously, which I had called "Neptune." At the dose 0.1, in a few minutes Neptune was defunct. It was so much the more surprising as even the dose of 1 kills only slowly, at the end of two or three days.

Of course, the experiment was repeated, modified, codified. It turned out to be the foundation of "anaphylaxie." As it was a new fact, I wished to give it a new name—a name which, like the word "zomotherapie" and the word "polypnee" has passed into the ordinary scientific vocabulary. These three new words signify three new things.

VI

Sometimes the preconceived idea, the working hypothesis, is almost true as it stands, but it has to be verified and corrected by experiment. Thus I said one day to my friend Hanriot "Chloral

is a hypnotic, so is lactic acid, let us see what chloral lactate will do—a combination of chloral and lactic acid. It ought to be a marvellous hypnotic." But alas, no! chloral lactate produced violent and terrible convulsions. Nevertheless, we were not discouraged. By combining chloral with an isomer of lactic acid, glucose, we obtained chloral-glucose which we named chloralose, a very interesting substance that can be employed as a hypnotic in human therapy, and which, meanwhile, is commonly used in laboratories today as an anaesthetic for animals.

But I must not prolong this story of the hesitations through which I passed in my various researches. If I have recounted them here, it has only been in order to show to what extent experiment is more fertile than imagination. The merit of the experimenter consists above all things in observing everything that happens, noticing the smallest details, in not being satisfied with plausible and unconfirmed conclusions although too often our intellectual idleness adopts them without examination.

Just one word to end this chapter—too personal, perhaps. It is a question of my method of working. I do not pretend that it is perfect, but I think that it has some merits, for it enables many experiments to be made rapidly. If I may employ a trivial comparison—a fisherman, in order to catch fish in a district of which he is rather ignorant, casts his line in various parts of the river. In the same way, it is necessary to try right and left all manner of experiments, one of which may perhaps be fruitful. But in order to do much, one must not delay too long over any one of these experiments. A first rough hasty one should be attempted, to see if it gives indication of immediate results. It would not be wise to apply laborious and complicated instruments to this attempt. One must find out, forthwith and very quickly, whether it is worthy of perseverance. If the result is nil, one does not continue, and will not have lost much time. But if one is successful, this first success is insufficient. Then ensues a long period of work, demanding a technique more and more perfect, instruments more and more precise. It is necessary to repeat and again repeat, changing all manner of conditions.

Moreover, it is necessary always to apply the most searching criticism. In so far as one has been hasty, elementary, unprecise at the beginning, one must redouble precision later.

No one has the right to encumber science with premature assertions I don't know which physiologist it was who said "An erroneous affirmation which has taken a day to construct, requires sometimes twenty years of work to overthrow" In his laboratory, before publication, the savant can be, and even ought to be, very rash, very rapid, but when it is a question of publication he must be scrupulous in the extreme

And I allow myself often to formulate the precept in this form "Be as bold in the conception of hypotheses as rigorous in their demonstration"

Original Contributions

PNEUMOCOCCAL PNEUMONIA

A Note on its Treatment with Sulphapyridine and Serum

By M J SHAH,

M B, M.R.C.P (Lond), D.T.M. & H (Lond)

(From the K E M Hospital, Bombay)

During recent years there has been a remarkable progress in the treatment of pneumococcal pneumonias, as a result of introduction of type specific serum therapy and chemotherapy. Previous to the use of these therapeutic agents, the average mortality of pneumonias in any hospital had seldom been below 20 per cent. Now the figures recorded vary from 5 to 10 per cent. The following are the figures for K E M Hospital, Bombay, for four years prior to the introduction of Sulphapyridine

TABLE I

Years	1935	1936	1937	1938	Present series
Total Pneumonia cases	611	504	523	700	150
Mortality	183 (29.9%)	154 (30.55%)	141 (26.9%)	204 (29.1%)	12 (8.12%)

Favourable results of sulphapyridine treatment have been reported from all over the world, (vide table No VIII). Favourable reports of serum therapy were mainly from America. In Bombay no attempt had been made to study the results of serum therapy, because of its unavailability and high cost. Prof Dhayagude prepared in Bombay type specific sera for use against infection by type I and type II pneumococci. Taking advantage of the availability of the serum, it was decided to study the treatment of pneumonia cases in three groups i.e. (1) those treated with Sulphapyridine alone, (2) those treated with serum alone and (3) those treated with both Sulphapyridine and serum combined.

With the above aim in view a scheme of work was evolved. A typed copy of the scheme was supplied to each and every house-physician, and the working of the scheme was explained to them. The following is the copy of the scheme of work

Scheme

"1 On admission of a case of Acute Lobar Pneumonia the House-Physician should send immediate information to Dr Dhayagude and Dr M J Shah. If they are not available the Resident Pathologist and Medical Registrar to Ward No 4 should be informed

2 A specimen of sputum should be sent to Clinical Laboratory for immediate typing (Typing done by Armstrong's rapid method)

3 A requisition for a total and differential count of leucocytes should be sent to the Clinical Laboratory

4 If the case belongs to type I or II pneumococcal pneumonia it should be treated alternately with serum alone, or with serum and M & B 693. If the case belongs to type III & group IV it should be treated on M & B 693 alone

5 Type I & II cases, to be treated on serum alone, should receive 20 c.c. of serum intramuscularly every 8 hours till 80 c.c. of serum are given in all (20 c.c. = 18,000 units)

6 The following routine should be followed for cases of types I & II with M & B plus serum —

An intramuscular injection of 20 c.c. of type specific serum to be given immediately after the result of typing is known. The serum is not to be repeated. Two tablets of M & B 693 4 times a day should be given for 2 days, to be followed by two tablets 3 times a day for one to two days, and then the dose should be diminished according to the condition of the patient

7 Symptomatic treatment should be given in the usual manner

8 Type III & Group IV cases to be treated on M & B 693 alone should receive the drug in the following doses —

2 tablets 4 times a day for 2 days, then

2 tablets 3 times a day for one or two days, and subsequently according to the need of the patient

9 It is essential that detailed notes of the cases should be kept from day to day, particularly from the point of view of good or bad effects of the different lines of treatment. The

Laboratory investigations in these cases should be attended to by the Clinical Pathological department"

The diagnosis of acute lobar pneumonia of pneumococcal origin was based on the usual clinical, laboratory and in some cases radiological findings

An analysis of a total number of 150 cases is reported below

Age — The age distribution was as follows —

TABLE II

Below 10 years	10-20 years	21-30 years	31-40 years	41-50 years	Above 50	Total
1	17	80	34	16	2	150

Of 150 cases 114 (76%) were in age group between 21 to 40 years showing greater incidence in young subjects 18 cases were older than 40 years

Sex — Of 150 cases observed, 145 were males and only 5 were females Though pneumonia is known to occur more commonly in males than in females, there must be other factors contributing for such a marked discrepancy

Day of Disease — The day of the illness on admission was as follows —

TABLE III

Day of disease	I day	II day	III day	IV day	V day	VII day	VII Or more	Total
No of cases	8	14	32	38	23	18	17	150

It will be seen that of 150 cases 54 (36%) sought admission within three days of onset, and 115 cases (77%) before 5 days of disease 17 cases that were admitted on 7th day or later of disease were not considered in evaluating the effect of either type of treatment, but were treated by the Honorary Physicians in charge Their treatment in these cases included M & B 693 in usual doses

Lobe Distribution — The distribution of the lobes affected by pneumonia were as follows —

TABLE IV

Side affected	Right side	Left side	Both	Total
Cases Present Series	75 (50%)	66 (44%)	9 (6%)	150
Cecil's cases	811 (42.8%)	666 (35.1%)	419 (22.1%)	1896

Of 150 cases, the disease was on right side in 75, on left side in 66 cases and on both sides in 9 cases. The lower lobes were affected in 128 (85 p c) of cases and the upper or right middle lobes in 22 cases giving a ratio of 6 : 1.

Types—Typing was done from sputum in all cases and showed the following distribution. If compared with the figures quoted by Haffron, there appears a relative infrequency of types I, II and III.

TABLE V

Type	I	II	III	Group IV	Not I & II	Not done	Total
Haffron's cases	32.8%	20.0%	10.8%	35.8%			
Present series	31 22.5%	11 9.1%	11 7.2%	81 51.9%	14	4	150
Dhavadgaude	7%	19.5%	5.7%	15%			

Thus less than a third (31.8 p c) of the total cases belong to type I and II, and are suitable for type specific serum therapy in the present series as compared to nearly 50 p c in Haffron's series. (In 14 cases marked 'Not I or II' the typing serum for type III was not in stock, while for 4 cases 'Not done' all sera were out of stock.)

Leucocyte Count—The total white blood cell count which was done in all cases at the beginning is shown in the following table.

TABLE VI

Total W B C per c mm	Less than 4,000	4,000 to 8,000	9,000 to 20,000	over 20,000	Total
Cases	4	25	100	21	150

Of 150 cases, 4 cases showed a count below 4000 per c mm, while 29 showed a count below 8,000 per c mm. It is interesting to know that out of a total number of 12 deaths 5 occurred in the group of 29 cases that did not show any evident leucocytosis.

Blood Culture—Blood culture was done at the beginning in 139 cases and was positive in 21 (15.1%) cases. Of these 21 cases, 8 belonged to type I, 2 to type II, and 11 to group IV. The relative infrequency of bacteriemia in this series as compared to other reported figures might be partly due to the fact that here the blood culture was attempted once only in each case.

X-Ray —The X-Ray of the chest was taken in 35 cases in all of which the X-Ray shadow coincided and confirmed the diagnosis regarding the evidence and the site of pneumonic consolidation. The skinograms showed areas of increased density at the site of consolidation.

Electrocardiogram —Electrocardiogram was taken in 29 cases (In majority of cases only one tracing was taken). The findings showed (1) tachycardia, (2) regular rhythm in all tracings, (3) PR interval 0.2 seconds in 2 cases, (4) low voltage in all leads in 7 cases, (5) QRS shaped like M in 1 case, and like W in 1 case, (6) T wave inconspicuous in 1 case, T inverted in 1 case and high positive T waves in 4 cases.

Therapeutic Results

Of the total of 150 cases treated under the scheme 101 cases were treated with sulphapyridine, 14 with combined sulphapyridine and type specific serum, 18 cases with type specific serum alone, 17 cases (admitted on the 7th day or later of the disease) were treated by the Honorary Physicians in charge. Their treatment included full therapeutic doses of Sulphapyridine. The total number of cases treated with serum, or with combined serum and sulphapyridine is small, because of the relative infrequency of cases affected by pneumococci type I and II in the present series. The results are tabulated in table No VII to show the effect of each type of treatment with reference to (a) presence of positive blood culture (b) effect of age above 40 years and (c) the type of pneumococcus.

(a) *Bacteremia* Out of the total of 150 cases, blood culture was done in 139 cases of which 21 showed presence of bacteremia. There were 3 deaths in 21 bacteremic cases, giving a mortality of 14.3 p.c. as compared to a fatality of 6.9 p.c. in cases with a negative blood culture.

(b) *Old Age* There were 18 cases belonging to group of age above 40 years, 6 of whom died giving a mortality of 33.3 p.c. for the age group.

(c) *Type* On analysis of mortality according to the type of infecting organism it was found that out of 34 cases of type I two died, of 14 cases of type II none died, of 3 cases of type III none died, of 81 cases of group IV seven died and of the remaining 18 cases 3 died.

The following table shows the therapeutic effects of the various modes of treatment as compared to one another

TABLE VII

	Sulpha pyridine	Combined (i.e. sulphapyri- dine plus serum)	Serum	Other routines	Total
Cases	101	14	18	17	150
Recovered	93	14	16	15	138
Expired	8 (8%)	Nil	2 (11 1%)	2 (11%)	12 (8%)
Bacteremic (Total)	11	7	7	2	21
Cases (Died)	3	Nil	Nil	Nil	3 (14 3%)
Age group above 40 (Total)	9	1	2	3	18
years (Died)	5	Nil	Nil	1	6 (33 3%)
Temp. normal in 1 day	49	8	2	2	
" in 2 days	68 (73 1%)	10 (71 4%)	7 (18 7%)	9 (60%)	
" in 3 days	80	11	5	12	
Temp. over 3 days	13	1	11	3	
Type I (Total)	9	11	12	3	34
(Died)	Nil	Nil	2	Nil	2
Type II (Total)	2	3	6	3	14
(Died)	Nil	Nil	Nil	Nil	Nil
Type III (Total)	2			1	3
(Died)			Nil	Nil	Nil
Group IV (Total)	60			1	81
(Died)	7			Nil	7
Not type I & II (Total)	9 (8+1)	Nil	Nil	9 (6+3)	18
and not done (Died)	1			2	3

Now let us consider each type of treatment separately

Sulphapyridine

A total of 101 cases were treated with M & B 693 tablets in the routine mentioned in the scheme. As seen in the table No. VII eight belonged to type I, two to type II, two to type III, eighty cases to group IV, eight cases to 'not type I & II, and in one case typing was not done. Of these 101 cases, 8 cases died giving a mortality of 8 p.c. A comparative table showing the results by various workers is shown below. It might be mentioned here that the eight deaths are inclusive of all deaths after starting the treatment (not excluding cases dying within 24 hours) as opposed to results quoted by some of the workers, where such deaths are not included.

TABLE VIII

Authors	No. of cases	Deaths
Agranat, Dreosti and Ordman	280	10
Findland, Spring, I owell and Brown	95	14
Gustford	400	26
Pepper, Flippin, Schwartz and Lockwood	500	38
Caplan	100	5
Homcke and Vogt	342	20
Yodh and Tulpule	80	6
Parekh, J. G.	230	14
Shah, M. J.	57	5
Present series	101	8

In these cases bacteriæmia was detected in 13 cases of which 3 died. There were 9 cases belonging to the age-group above 40 of which 5 died.

Of the 93 cases that recovered temperature came down to normal in 24 hours in 49 cases, and within 48 hours in 68 (73 p.c.) cases.

This compares favourably with figures quoted by other workers.

Of the 93 cases that recovered 6 cases showed some complications. There was a secondary rise of temperature lasting for a day or two in 4 cases, a delayed resolution in 1 case and formation of an acute lung abscess in 1 case. There was no other complication excepting occasional nausea and vomiting. There were no serious drug complications in any one of the cases treated. Thus it could be seen that the toxic effects of the drug were not encountered when the drug was given in the dosage indicated, without in any way affecting the therapeutic results.

Dosage—The dose of sulphapyridine administered in these cases was two tablets (1 gm.) four times a day for two days, two tablets three times a day for a day or two, and subsequent gradual reduction according to the need of the patient. On an average a total dose of 30 to 40 tablets (15 to 20 grms.) was administered. This dosage is "moderate" as compared to the high dosage advocated by other workers.

Evans and Gaisford (1938) advocated a routine dosage of two grams stratum and one gram four hourly thereafter, making an average total intake of 25 gms. (50 tablets) in an average case of pneumonia. A higher dose was given for serious cases.

Plummer and Ensworth (1939) gave an initial dose of two grams (4 tablets) followed by one gram four hourly until 16 grams were given, at that point they again decided whether the drug was to be discontinued or not. Others advocate still higher doses.

The dose used in the present series is smaller than the one used by above authors, and hence the term "moderate" is used for it.

The workers who advocate an "intensive" system of dosage claim that it has the advantage of rapid saturation of the drug in the blood. Long and Bliss (1939) advocated concentration of the free drug in blood of 4 to 6 mgms per 100 c c for effective therapy in moderate cases, and 7 to 10 mgms per 100 c c in severe cases. Abernethy, Dowling and Hartman (1940) recommended a mean drug concentration of 6 mgms or higher per 100 c c of blood.

But Harrison (1941) and his coworkers, who made an attempt to co-relate the drug level in the blood with the dropping of temperature by crisis in pneumonia cases treated with sulphapyridine, found that a satisfactory response was obtained with drug concentration ranging from 2 to 15 mgms per 100 c c of blood. They also found that the therapeutic response in patients with drug concentration below 6 mgms, when compared with those having the drug concentration above 6 mgms did not show any significant difference.

Plummer and Ensworth (1939) using the routine usual dosage quoted above obtained blood levels of free drug ranging from traces to 25 mgms per 100 c c. Some of the best therapeutic response occurred in 'lowest blood level group'. In several of their cases which did not show a prompt response, an increase in dose had no effect on clinical course.

Flippin and his associates (1939) tried to find out whether there was any co-relation between the rapidity of the recovery and the concentration of free sulphapyridine in the blood. They compared 11 cases showing blood level of 1 to 2.8 mgms (lowest group) of the free drug, with other group of 11 cases showing a blood level of 10 to 18 mgms (highest group) and found that 9 out of 11 patients in the lowest group showed critical drop of temperature in 24 hours, opposed to 6 out of 11 cases in highest group. Also, the total duration of the disease compared favourably in both the groups.

Kohlstaedt and Irvine (1940) concluded that they had been unable to establish a direct relationship between the dose administered and the concentration of free sulphapyridine in blood. Several times the patients who received smaller doses, showed higher concentration of the drug, while higher doses failed to raise the blood level in other cases. Many of their

patients recovered when maximum blood concentration of free sulphapyridine was less than 3 mgms per 100 cc of blood. They also concluded that high concentration of the drug did not always mean recovery because three of their fatal cases showed drug concentrations of 18 mgms, 14 mgms and 11 mgms per 100 cc respectively. Further the high drug concentration did not ensure freedom from complications as showed by one of their patients, who developed empyema with a blood level of 6 mgms per cent of free sulphapyridine and the aspirated fluid containing 3 mgms per cent of the drug.

From these findings it is clear that the optimal blood concentration of the drug for maximum therapeutic response for pneumonia is not conclusively worked out, and that a satisfactory response is obtained over a wide range of the blood level of the drug. The dosage used in the present series is not an 'intensive' one, but may be termed 'moderate'. The therapeutic results compare favourably with those reported by others. Also it has the advantage that the toxic effects of the drug were rarely encountered. Brown (1940) and coworkers observed higher incidence of toxic effects when high concentration of the drug occurred in the blood and concluded that dosage on a lower scale than the one widely used could be administered without loss of therapeutic effect, and with less frequent toxic manifestations.

Serum Treatment — 18 cases were treated with serum alone. Of these 12 belonged to type I and 6 to type II. Two cases died. They both belonged to the age-group below 40 years. Bacteriemia was detected in 3 cases, all of whom recovered. Of the 16 cases that recovered, temperature came down to normal within 24 hours in 2 cases. In 11 cases it persisted for more than 3 days. Thus the rapidity of crisis does not compare favourably with sulphapyridine cases. Complications mainly consisted of secondary rise of temperature in three cases, serum arthritis in 2 cases, and marked meningism in one case. The serum was administered within 3 days of the onset of illness in 10 cases, and later than 3 days in 8 cases. There was no mortality in the first group. Both the fatal cases were treated with serum after the 4th day of the disease.

Though it is not possible to arrive at definite conclusion regarding the efficacy of serum, it seems to be effective in lower-

ing the mortality if given early in the course of the disease, though it does not seem to have favourable effect on the duration of fever when compared to sulphapyridine. Also serum seems to be more effective in persons belonging to age-group above 40 years, and in bacteriemic cases as compared to sulphapyridine. A good percentage of cases developed serum reactions.

Combined Treatment—14 cases were treated with combined sulphapyridine and type specific serum. The serum was given as an initial dose of 20 c c intramuscularly and was not repeated. Then the patients were treated with sulphapyridine alone. There was no mortality in this group. The number of cases treated with combined treatment is too small to enable one to come to any definite conclusions. Of the 14 cases 11 were affected by type I and 3 by type II pneumococci. 3 cases (21.4 p c) showed presence of bacteremia, and 4 cases (28.5 p c) belonged to age group above 40 years of age. The temperature came down to normal within 24 hours in 8 cases and within 48 hours in 10 cases (71 p c). There was presence of secondary rise of temperature in 3 cases. No other complications were met with in this series. It appears that the combined treatment with an initial dose of type specific serum to be followed by moderate dose of sulphapyridine promises better results in cases of pneumococcal pneumonia.

Comparative table is given below—

TABLE IX

	Cases	Deaths
Pipper, Flippin, Schwartz and Lockwood	12	2
Cutts, Gornally and Burgess	17	3
Plummer and Insworth	102	16
Schwartz, Flippin and Turnbull	14	1
Present series	14	Nil

Discussion—It is the experience of every clinician that acute lobar pneumonia when treated with recent therapeutic measures, carries a better prognosis as compared to a few years ago. Today there are two specific remedies—the chemotherapy and the type specific serum therapy. Though both these methods show a reduction in mortality of pneumococcal pneumonia, the mode of action of each is different. The mechanism of action of sulphapyridine shown by animal experiments in mice by McIntosh and Whitby is to be ascribed to bacteriostasis or inhibition of bacterial growth.

They showed that the drug did not affect 'the quality, quantity or speed of production of recognised anti-bodies' Hence the cure in cases treated with the drug is due to the combined effect of chemotherapeutic bacteriostasis and the defensive mechanism of the patient himself While the type specific serum acts in view of its immune bodies Hence on experimental grounds the combined treatment with drug and type specific serum should be more effective than either agent alone This conclusion is supported by the clinical trial in the present series Though the number of cases so treated is small, the difference is quite apparent In combined treatment perhaps a smaller dose of each remedy would be necessary In the present series serum was given only as an initial dose of 20 c c while sulphapyridine was given in the same 'moderate' doses as in other cases

Other routines—17 cases that were admitted on the 7th day of the disease or later and which were not included in the study, were treated by the Honorary Physicians in charge of the cases Their treatment included full-doses of M & B 693 The results would not be strictly comparable because of the late admission Of the 17 cases, 2 died and 15 recovered The temperature fell to normal within 24 hours in 7 cases and within 48 hours in 9 cases Bacteriemia was present in two cases Three cases belonged to age-group above 40 years, one of whom died There was presence of secondary rise of temperature in 2 cases

Conclusions and Summary

(1) A note is presented on 150 cases of Acute Lobar Pneumonia treated at the KEM Hospital with a view to compare the therapeutic response by (1) sulphapyridine in moderate doses (2) type specific serum and (3) combination of sulphapyridine and serum

(2) Treatment with sulphapyridine in "moderate doses" was tried in 101 cases, giving a mortality of 8 per cent and showing no toxic effects Moderate doses show good therapeutic efficacy and absence of drug toxicity or of other complications Cases showing (1) bacteriemia and (2) cases belonging to age-group above 40 years of age show a comparatively higher mortality in this group

(3) Type specific serum treatment was tried in 18 cases in total dosage of 80 cc (20 cc = 18,000 units) intra-muscularly, with a mortality of 2 cases. Though the therapeutic effects of serum is favourable the fever takes longer time to settle down, and there are serum reactions. But serum therapy seems to be particularly effective in (1) bacteriemic cases and in (2) cases above the age of 40.

(4) Combined treatment with (1) sulphapyridine and (2) type specific serum was tried in 14 cases with no mortality. In view of experimental and clinical data showing marked improvement in therapeutic results, a plea is made to give further clinical trial to such combined treatment.

I take this opportunity to thank Dr. Jivraj Mehta, the Dean of K. E. M. Hospital and all the Honorary Physicians who gave me full opportunities to present this small note. All credit for laboratory investigations goes to Professor Dhayagude and the pathology department staff. The Medical Registrars Dr. V. V. Shah and Dr. S. C. Sheth have rendered great help to me. My thanks are due to them and to all other Resident Officers who have helped me.

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A paper read before the Staff Meeting of the C. S. Med. College and the K. E. M. Hospital, Bombay, on 14 March, 1942.

Case Reports

AN UNUSUAL CASE OF CORONARY THROMBOSIS

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BOMBAY

The following case of coronary thrombosis presents features sufficiently unusual to warrant publication —

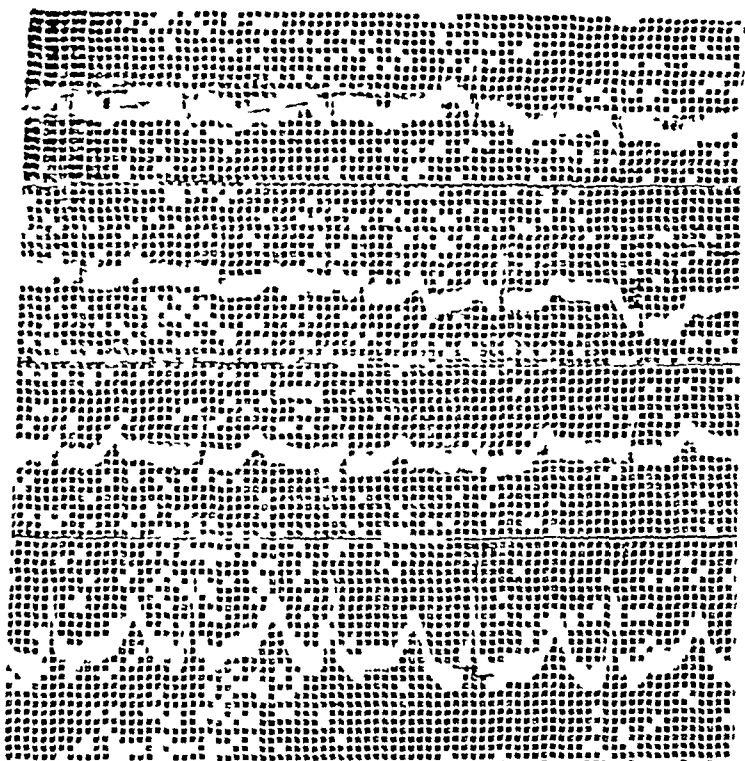
A Parsee gentleman, aged 64, clerk in a firm of solicitors, was seen for the first time in September, 1940, with a history of asthma for years. A few years ago, he had been given NAB intravenously for the asthma but the injections had to be abandoned on account of an exfoliative dermatitis in both arms.

Since the beginning of 1940, he had been getting increasingly short of breath, his discomfort was worst on climbing stairs, walking uphill and after bouts of coughing. He had also been subject for some months to an unusual type of angina. The pain, which came on during or immediately after exertion, was invariably preceded by a prodromal sensation (or "aura"), "a tugging sensation" at the posterior part of the right border of the tongue. The anginal pain was always confined to the right side of the chest (never extending to the left of the sternum), most marked in the third and fourth intercostal spaces about 2 or 3 inches to the right of the sternum. Radiation of pain was noted to a corresponding point on the right side of the back and along the inner aspect of the right arm to the elbow. Pain was never bilateral. Substernal oppression and "angor animi" were unknown to the patient. The pain would last for 1 to 10 minutes only. His average blood pressure used to be 140 to 150 mm Hg (Systolic).

On the 5th December, 1940, while reclining after day's work, he suddenly experienced a pain and "tugging sensation" in the right border of the tongue. This was accompanied by a "heavy pain" in the right side of the chest, front and back, the pain was most intense in the 3rd, 4th and 5th right interspaces, about 3 inches from the midline. There was no substernal oppression, no dyspnoea and no fear of death. There was feeling of intense nausea with repeated vomiting and extreme degree of restlessness. The peculiar sensation in the tongue and the chest pain lasted throughout the night and the next day. About 2 hours after the attack the B.P. was 158 mm Hg and 12 hours after the attack, it was 148 mm Hg, there

was no evidence of collapse. On the evening of the 6th, his B.P. had fallen to 118 mm Hg. While the pain had diminished considerably.

The apex beat was in the fifth left interspace, 4 inches from the midline. The 1st sound at the apex was rather feeble. No rub was audible. An electrocardiogram (see fig.) showed evidence of coronary occlusion (anterior type). On the morning of the 7th, the pain had disappeared except for a small region in the back, the B.P. had fallen to 100 mm Hg systolic and restlessness was intense. In the afternoon, he complained of an instant urge to evacuate his bowels and asked for a bedpan. After a moment or two of intense depression, he expired suddenly.



FIG

A 4 Lead Electrocardiogram showing inverted T waves in Leads I and IV, depression of S-T segment in Leads II and III, doming of S-T in Lead IV, prominent Q waves in Leads I and IV and low voltage curves in all standard leads.

The Electrocardiographic findings suggest Coronary occlusion of the anterior type.

Discussion

This case displays the following interesting features —

(1) Localisation of pain to the right side of the chest. In this case, both types of pain viz the anginal seizures and the pain of coronary thrombosis, were restricted to the right side of the chest.

Though the distribution of anginal pain, in the great majority of instances, is distinguished by its sinisterity (or localisation to the left side of the body), cases are not rarely encountered where the pain is

bilateral or right-sided I have personally observed atleast four cases with anginal pains strictly confined to the right side of the chest. Such unusual sites for anginal pain need not necessarily stop us from diagnosing the pain as anginal provided certain other characteristics of anginal pain are observed e.g. relationship to exertion, immediate response to rest and nitrites, substernal discomfort, nature and duration of the seizure, co-existence of heart disease etc.

Cowan and Ritchie² found radiation of anginal pain into the right arm alone in 2 of their series of 200 cases, while in 24 cases the pain radiated into both arms. According to Paul White¹¹ radiation of anginal pain into the left arm is about 25 to 50 times more frequent than radiation into the right arm.

The normal left-sidedness of anginal pain is in accordance with the anatomical arrangement of the fibres of the afferent sympathetic cardioaortic pathway. Impulses of pain from the heart and aorta are transmitted by sympathetic fibres that enter the upper four thoracic levels of the spinal cord (Thoracic 1 to 4), on the left side. In order to understand the reference of cardiac pain, it is important to realize that these very levels of the spinal cord (viz, Thoracic 1 to 4) receive afferent somatic neurones from the left side of the chest and the left arm dermatomic zones).

Since these two independent sets of impulses, from the heart and aorta on the one hand and from the left side of the chest and arm, meet or triangulate at a common locus of convergence within the substance of the substantia gelatinosa Rolandi of the spinal cord, mediation of referred pain occurs at this point of convergence. Pain sensations, picked up at this focus, are transmitted by the spinothalamic tracts to the cortex cerebri.

Though the majority of cardiologists believe in an intra-spinal mediation of referred pain i.e. in the region of the substantia gelatinosa Pike⁹ and Danielopolu¹⁰ are strong supporters of the theory of extra-spinal mediation of reference.

Right sided radiation of anginal pain (as in this case) may be explained by assuming a preponderance of dextral sympathetic fibres leading from the heart to the right side of the spinal-cord, instead of the left side as in the majority of instances. Whether dextral fibres are over-active or unduly developed in such individuals or whether sinistral fibres are under-active for some reason or other, it is difficult to say. Since the innervation of the heart is bilateral, there is no reason why the fibres on the right side should not carry impulses of pain to the brain in some cases. In a case of angina described by Danielopolu and Danulesco⁴ radiation of pain to the right side was observed and attributed to congenital dextrocardia with transposition of all viscera.

Though radiation of pain to the right side of the chest has frequently been described in cases of angina, previous case-reports of coronary thrombosis with pain strictly confined to the right side of the chest, have not come to my notice. One is therefore inclined to regard the right-sidedness of the pain in the present case of coronary thrombosis as an extreme rarity.

(2) The "tugging sensation" and pain in the back of the tongue were constant premonitory symptoms in this case. Pain in the back of the tongue is, like other regions of reference in the head and neck, probably due to the transmission of nervous impulses by accessory sympathetic afferent fibres⁶. Such fibres have been described in man by Heinbecker⁶ and others. It is quite likely that in the same individuals, these accessory channels may be sufficiently well-developed to act as accessory routes of pain. Subjective reactions or prodromal symptoms of this nature, though commonly presaging or heralding the commencement of anginal seizures, have received but fragmentary mention from writers on the subject. Their importance has been recently stressed by Hyman and Parsonnett⁷. These subjective sensations roughly correspond to the "aura" of epilepsy. They may be experienced in widely separated areas of the body e.g. face, neck, shoulder, arm, fingers, jaw, tongue, ear, eyeballs, nostrils or even the rectum, a few minutes before the actual seizure of angina. Nervous pathways capable of transmitting cardiac pain into zones of uncommon radiation like the tongue, have not as yet been properly worked out.

(3) Another interesting feature in this case is the early rise of blood-pressure with a delayed fall. In the great majority of cases of coronary thrombosis, the blood pressure shows a marked drop, soon after the attack, this drop of pressure has justly been regarded by clinicians as one of the most diagnostic of the clinical features of coronary occlusion. Though a fall of blood-pressure, both systolic and diastolic, constitutes one of the most constant features of the altered haemodynamics of coronary thrombosis, it may fail to appear in rare cases.

According to Hyman and Parsonnett,⁷ cases of coronary thrombosis display two drops of blood pressure, the first fall in pressure occurs during the second hour after the onset of the attack, the second fall of pressure usually occurs in the 12 to 18 hour interval following the onset of the thrombosis. The initial fall of pressure may fail to appear in a few cases of coronary thrombosis, in such cases, the blood pressure sign loses its diagnostic value, atleast for the first twelve hours or so after the attack. Weiss¹⁰ contends that the blood pressure may be actually higher than normal during the early painful phase of a coronary attack. There are a few observations in the literature on this early rise of blood pressure in cases of coronary throm-

bosis Fitz⁵ reports a case with early rise of blood pressure Barker¹ makes allusion to this early rise of pressure in his paper. More recently Weiss¹⁰ has reported three cases of coronary occlusion with the early rise of blood pressure. In the present case, a rise of about 20 mm Hg above the normal level was observed soon after the attack.

The cause of this early rise has been simply explained by Weiss¹⁰. He suggests a production or initiation of pressor reflexes in the early stage of coronary occlusion by the pain, restlessness, anxiety and other mental disturbances. He also suggests as a subsidiary cause of the rise, a compensatory increase of peripheral vascular resistance, such as occurs in case of left ventricular failure or shock.

(4) A "feeling of rectal distension" or an immediate urge to evacuate the lower bowel, as was observed in this case, is not a very rare symptom of cardio-vascular disease. I have personally observed this feature in the following types of cases —

- 1 Acute coronary thrombosis,
- 2 Acute pulmonary embolism,
- 3 In Angina Pectoris, as an "aura" or premonitory symptom.

In the majority of cases, this "feeling of defaecation" occurs as a preterminal event, a few minutes or seconds before death. Hence, this symptom should be viewed with anxiety when encountered in cases of coronary occlusion or pulmonary embolism.

Summary

A fatal case of coronary thrombosis is presented for the sake of certain unusual clinical features. Particular attention is drawn to the right sidedness of the chest-pain, the initial rise of blood pressure and the peculiar subjective sensation in the region of the tongue.

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Analytical Review

PREVENTION OF DIABETES MELLITUS

By

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In modern times, the practical wisdom contained in the old maxim "Prevention is better than cure," is universally recognised. The preservation of the health of the population is now considered to be a matter of equally vital importance as the national defence of the country or its internal police supervision. The state and municipal health authorities are taking more and more interest in the prophylaxis of diseases on account of altered public opinion at one time so sceptical and antagonistic. Besides, researches all over the world are nowadays undertaken more and more with a view to study the causes and means of prevention of disease rather than to study its therapeutics.

As a result, the field of preventive medicine which at one time was restricted to a comparatively few diseases chiefly of a communicable nature has greatly been widened, and today a comparatively large number of diseases such as Malaria, Syphilis, Tuberculosis, Small pox, Plague, Rickets etc.,—formerly regarded as serious menaces to mankind—have greatly been brought under control, and some of them, if not all, can claim to be definitely classed under "Preventible Diseases."

On the other hand, there are several diseases notably Cancer, Rheumatism, Gout, Diabetes Mellitus, and various anaemias which still flourish and exact an appalling toll of deaths. They still provide very vexatious problems to the students of preventive medicine especially, when causes of many of these diseases are at present very little known or understood. However in several cases, satisfactory methods of diagnosis and treatment have luckily been found.

Diabetes Mellitus, seems to have existed over two thousand years and yet its causation is very little understood and remains a subject of much speculation and research. This disease is definitely known to have afflicted mankind since very remote times, even before the Christian Era, references to it being found in the writings of early medical authorities. The name Diabetes (Dia=through and benem=to flow) by which the disease has ever since been known, was given by Aetaceus—a Greek physician of the 2nd century.

The adjective Mellitus (=Sweetish) was added to "Diabetes" much later, in about the middle of the 18th century. It was first used by Cullen to differentiate cases of saccharine polyuria from those of a benign nature known as Diabetes Insiptidus in which excessive amounts of urine without sugar were passed.

It is a matter of common knowledge that Diabetes was known and its symptoms studied by the ancient physicians of India. It is believed to have been first described by Charak, but it was however Sushrut (500 A.D.) who noted and described for the first time, the sweetness of diabetic urine and gave the name मधुमेह (=Honey Urine) to the disease.

History has revealed that from the earliest times, till the present day, Diabetes has attracted the attention of medical men of all ages and all climes, and has provided to scientists, both clinicians and laboratory workers—a fascinating but rather a puzzling theme for intense research and a close study.

Diabetes Mellitus may be defined as "a chronic constitutional disorder (probably hereditary) characterised by impaired ability of the body to burn sugar associated with a tendency to subsequent disturbances of protein and fat metabolism and clinically manifested by (1) Hyperglycaemia i.e. increase of sugar in the blood and (2) Glycosuria i.e. excretion of sugar in the urine.

Rising Incidence of Diabetes Mellitus

There prevails the belief that Diabetes Mellitus is one of the many curses of modern civilization and that its incidence all over the world has slowly but markedly risen during the last 50 years. It is stated that about 0.3 per cent of the total population of the United States is affected with Diabetes. The increase has been ascribed and perhaps rightly, to gross gastronomic indiscretions coupled with sedentary habits and increasing worries that are imposed by the conditions of our modern, hectic city life.

The exact information as to the incidence of Diabetes Mellitus is scanty and the only evidence at present available to indicate its extent is furnished by the study of deaths ascribed to the disease. They have markedly increased in number in almost all civilized countries in spite of recent advances in the treatment made possible by the discovery of Insulin and the newer knowledge in the physiology of food.

In the United States, Diabetes Mellitus in 1934 occupied the 9th place as the cause of death as against 27th place in 1900 (Joslin)¹. It is stated in the Registrar General's reports for 1936 that in England and Wales deaths from Diabetes were steadily rising and were as numerous as those from all infectious diseases put together (Lancet 26-2-38). Dublin (1930) opined that "Within 10 years, Diabetes would equal Tuberculosis as a cause of death". Figures given in table No. 1 clearly indicate the upward trend in the diabetic death rate all over the world perhaps with the exception of Japan.

TABLE No 1
Death rate of Diabetes in certain countries

Country	Death rate per 100,000			
	1870	1920	1930	1934
United States	21	16.1	19.0	22.1
England & Wales	8.6	10.0	14.2	16.0
Scotland		9.0	12.5	15.0
Denmark		12.5	14.5	18.3
Switzerland		7.7	11.0	15.3
Sweden		11.5	13.1	11.2
Austria		11.5	11.2	15.7
Italy		4.5	8.2	9.5
Japan		3.1	3.5	3.9
India		—not available—		

Figures for India are not available, still there are good reasons to believe that they far exceed those for any of the western countries with worst incidence

Defective Registration of Deaths

Statistical figures mentioned in the above table though very suggestive of the rapidly increasing incidence of Diabetes do not reveal its fullest extent. On account of the defective registration of deaths, specially in India, the number of deaths recorded under Diabetes does not actually represent the total number of persons with Diabetes who die.

On the other hand, it has been argued that the increase in the incidence of diabetes is only apparent and not real for reasons which are as follows—(1) That during the past 50 years the expectation of life of the population at birth has considerably increased (ageing of the population) and this means that more people reach the middle period of life—a period during which there is increased susceptibility to diabetes. Hence an ageing population means an increased prevalence. (2) That Insulin has enabled many diabetics to live much longer than before and they help to swell the number of diabetics living and (3) That increased number of doctors, increased facilities for diagnosis and treatment and compulsory medical examination for admission into many kinds of services and for insurance purposes have helped to bring to light many more diabetics who would have otherwise escaped being detected.

However, it is the considered opinion of many that there is an absolute increase in the incidence of diabetes during recent years, perhaps much more than it is commonly imagined.

Deaths from Diabetes in the Presidency and City of Bombay

It may be noted as well that deaths both in the presidency and the city of Bombay have increased nearly twice as many during the last ten years.

Table No 2 shows the number of total deaths as well as those from diabetes that occurred at the different government hospitals and dispensaries in the Bombay Presidency during certain years.

TABLE No 2 *

Year	Total No of deaths	Diabetic deaths
1927	7334	17
1930	8576	28
1934	8754	35
1935	8377	36

* Administrative reports of the Surgeon General to the Government of Bombay

In the city of Bombay deaths from diabetes have steadily increased in number during the last 15 years. They have in 1936 equalled those from automobile accidents which are reported to be 88 in number¹

TABLE No 3 †

Shows total deaths as well as from diabetes in Bombay city

Year	Deaths from all causes	Deaths from Diabetes
1925	31968	38
1926	31999	34
1927	27655	43
1928	27312	60
1929	26555	73
1930	27552	64
1931	25105	71
1932	22858	75
1933	27174	79
1934	27370	92
1935	29289	97
1936	29934	87

† Bombay City Municipality Health Officer's reports for the years 1925-1936

TABLE No 4 **

Showing the number of patients treated and number of deaths from diabetes at the K E M Hospital

Year	Total No of pts admitted	No of diabetic pts admitted	No of Diabetic in patients	No of Diabetic deaths
1926-27	515	15	19	2
1927-28	512	19	12	2
1928-29	828	27	33	5
1929-30	917	31	57	6
1930-31	1012	31	79	3
1931-32	997	56	47	6
1932-33	917	62	62	4
1933-34	1010	70	68	5
1934-35	1044	59	63	6
1935-36				

¹ Administrative reports of the Police Commissioner Bombay, 1937

** Administrative reports of the K. E. M. Hospital Bombay

secondary disturbances in protein and specially fat metabolism occur and are apt to prove of greater danger than the original disorder. For this reason, the necessity for detecting and treating early cases of diabetes cannot but be over emphasized. The maxim "A stitch in time saves nine" holds too true in the case of diabetes and must always be remembered.

Blood Sugar in Diabetes

In the mild cases, the blood sugar when fasting may be within normal limits, but the administration of 100 to 150 gms of glucose raises it from the normal 0.1 to 0.12 per cent to a much higher level—0.2 per cent or more. The maximum height is reached in about 1.2 or 3 hours and the blood sugar also takes a comparatively long time to return to its normal level, (Lag Curve). Whenever the blood sugar rises above the normal kidney threshold or the leakage point viz 0.18 per cent kidneys begin to excrete sugar and in this way help to maintain the blood sugar within normal limits. In the more severe cases however, the blood sugar is always above the normal kidney threshold and sugar is excreted throughout the day.

Primary Disturbances

As regards the actual nature of the disturbances it is believed that there is an interference in the aerobic oxidation of glucose in the tissue—the main point of Insulin attack, the degree to which glucose oxidation is reduced is proportionate to the severity of the disease, in other words, to the deficiency of Insulin.

It is believed that the anaerobic part of glucose oxidation upto the formation of lactic acid takes place normally in diabetes (Loebel, Barre Tolstoi and Himsworth—1924) but that it is the subsequent aerobic oxidation of lactic acid which is inhibited. This reduced oxidation is manifested by a reduction in the Respiratory Quotient which in a diabetic seldom approaches the normal viz, 1 after a meal, and is usually 0.8 or somewhat below it.

The resynthesis of glycogen from lactic acid in the muscle is greatly reduced on account of the reduced oxidation of lactic acid, this explains why muscles are frequently found to contain smaller amounts of glycogen as the disease progresses (Peters, Van Slyke 1931). The heart muscle at first is not much affected but later suffers from the effects of reduced oxidation and gradually becomes enfeebled.

The lactic acid which is not utilized by the muscles is transferred to the liver and may there be synthesized into hepatic glycogen. This is the reason why the lactic acid content of the blood is not much increased in early and mild cases of diabetes. Later, the liver loses its power to store glycogen and contains during the terminal stages of the disease a nominally small amount of glycogen, though it is never found completely empty even in fatal cases of coma.

In spite of the increased presence of glucose in the blood the tissues behave as if there is very little glucose and an increased demand for sugar is made on the liver which in its turn responds by increased rather than diminished conversion of glycogen into glucose (glycogenolysis) (E Lesser 1923, Lesser and Zilt 1923, Hedon 1928) The enlarged liver which is occasionally seen in the later stages of the disease is not due to the increased quantity of glycogen but due to its infiltration with a large amount of fat

Secondary Disturbances of Fat and Protein Metabolism

As long as the carbohydrate metabolism alone is affected the disease pursues a relatively benign course, but the great danger arises when with the progress of the disease, especially in untreated cases, secondary disturbances in protein and fat metabolism set in resulting in their abnormal destruction

There is an abnormal increase in the break down of fat which is manifested by an increased neutral fat content of the blood (lipaemia) with a simultaneous rise in cholesterol-esters and phospho-lipids Fatty infiltration also takes place in various organs including liver and heart Blood vessels are also affected with arterio-sclerotic changes a little later

When sugar is burnt incompletely as in Diabetes Mellitus, the oxidation of fat stops short perhaps at the poisonous aceto-acetic acid and para-oxy-butyric acid stage These acids accumulate in the blood and produce a condition which is called ketosis or acidosis (a wrong name) In this condition, there is a marked fall in the amount of CO_2 in the alveolar air with a simultaneous increase in the tissues As a result, the respiratory centre is depressed and the patient gradually passes into a comatose condition The patient can recover from this condition provided administration of Insulin in rather heroic doses together with large amounts of glucose and fluids, is started quite early

The protein of the food and the body tissues are next attacked and broken down in abnormally large quantities in an attempt to supply more glucose and more anti-ketogenic materials Proteins may be metabolized into glucose to the extent of 58 per cent and help to produce a further rise in the glucose content of the blood Also certain amino-acids of the protein molecule may be converted into beta-oxybutyric acid and aceto-acetic acid and may cause a further increase in ketosis

Manifestation of Diabetic Intoxication

The patient gradually loses much in weight and strength in proportion to the severity of the disease on account of excessive destruction of the tissues There is also an increase in the output of urinary nitrogen which may greatly accumulate in the blood and produce the fatal uraemia The body suffers from great reduction in its alkali reserves as well as from considerable loss of water (dehydration) due

to voiding of large quantities of sugar and ketone bodies. Last of all, the circulation is much impaired on account of the diminished volume of blood and enfeebled heart and urine secretion becomes scanty or suppressed. Toxic waste products both nitrogenous and ketogenic, accumulate and complete the picture of "diabetic intoxication."

THE ETIOLOGY OF DIABETES MELLITUS

"the fields of etiology and prevention of diabetes are contiguous and that the inference to be drawn from a survey of one makes almost unnecessary a survey of the others"—Joslin

There is much confusion of thought as regards the etiology of diabetes. In spite of great painstaking investigations carried over several decades of years, diabetes mellitus still remains one of the many diseases for which no satisfactory cause has been found.

Though deficiency of Insulin either absolute or relative has clinically, pathologically and experimentally been proved to be the immediate cause of diabetes, still it is not known what causes deficiency of Insulin secretion, whether the deficiency is qualitative or quantitative or whether the pancreas is primarily at fault or otherwise.

Pancreatic Disorders

The association of Diabetes Mellitus with pancreas was suspected since long, on account of repeated finding of morphological changes in that organ by a number of independent observers (Von Brunner 1683, Cawley 1788, Bright 1837, Von R. Huussen 1864, Bouchardt 1851, Lancereau 1877, Flerichs 1884). In 1889, Von Mering and Minkowski by their classical experiments definitely showed that in dogs, a diabetic condition was produced by removal of the pancreas. Further, Minkowski (1906) and later Hedon demonstrated that this experimental diabetes could be prevented by pancreatic grafts. This work conclusively proved that the pancreas produced an internal secretion, the lack or deficiency of which was responsible for the diabetic condition. Later on, it was shown that this secretion was produced by the cells in the Islets of Langerhans (Laguesse) and that these cells underwent degenerative changes in diabetes (Opie 1901, Ssobolew, MacCallum and others). This theory of pancreatic or more correctly Insulin deficiency, first championed by Sauerbeck (1904) and still accepted today at least as a working hypothesis for treatment purposes, seemed almost complete when Banting and Best isolated and prepared in a pure form, Insulin—the long sought for hormone of the pancreas—which when injected, brought about at least a temporary alleviation of symptoms both in experimental and human diabetes during the period it lasted in the body.

Though Insulin has revolutionized the treatment of diabetes, it has not yet helped materially to determine the exact cause of the disease, and the bright hopes engendered by the discovery of Insulin for an early and complete elucidation of the causation of diabetes still remain to be fulfilled.

Finding of abnormal distribution of glycogen and success of Insulin therapy in both experimental and human diabetes, have undoubtedly marked out Insulin deficiency as the sole immediate cause of diabetes. This deficiency of Insulin—the blood-sugar-reducing principle elaborated by pancreas may be actual (1) through its secretion being either lessened in quantity or changed in quality or (2) through neutralization of the secretion by some hypothetical substance after Insulin is normally secreted or (3) by failure of transportation of the secretion from the islands. The deficiency may on the other hand be relative (1) through increased demand or (2) through insufficient facilities for formation and storage of glycogen (as for instance in the liver disease). We are still in dark which factor or factors are responsible for the supposed insufficiency of Insulin. This question of Insulin insufficiency is not likely to be settled till such time when tests for estimating Insulin in the blood or urine are successfully devised.

Moreover, the post-mortem study of the anatomical and microscopical lesions of the pancreas has not been found instrumental in elucidating the cause of the disease. Opinions have differed as to frequency and nature of the recognizable changes found in the organ. At one end of the scale, we have the readily understood cases of diabetes following extensive destruction of the pancreatic tissues and at the other end, we have cases which are difficult to explain on account of absence of any demonstrable pathological lesions in the pancreas as in the case of a child died of diabetes. Further, pathological lesions found in the pancreas cannot often be attributed to any known cause such as calculus, new growth or acute or chronic pancreatitis. The mechanism by which the selective lesions in the island cells occur is obscure, it is not possible to say whether they are due to any infective organism or any toxin circulating in the blood or are, as is believed in the case of hydropic degeneration of Island cells, the result of functional over-strain.

Because of great liability to arterio-sclerotic changes in diabetes hyalinization of the Islands in the older diabetes, is to be associated with the arterio-sclerotic changes in the Insular blood vessels. But how far the vascular changes contribute to the development of diabetes is not known.

Regeneration of Island cells

The presence of normal Island cells in the diabetic pancreas has always been a source of discussion and conjecture. In fact, even in the severest forms of the disease, the islands have never been found completely diseased or destroyed. It is one of the many suggestions, more or less based on experimental evidence that Island cells do not submit tamely to injury but always endeavour to replace diseased or destroyed cells by means of increased proliferation and that new cells are formed in the periphery of the Islands (Warren, Cecil, Weichselbaum and recently Richardson and Young 1938). This explains the

gradual and insidious development of the disease through slow but progressive destruction of the islands and the failure of regeneration of the Island cells to make good the loss. If we accept this theory, it becomes easy to explain the preservation and very often improvement of sugar tolerance over long periods in carefully treated cases, especially the young diabetics, and also to bring home the fact that in the anti-diabetic fight, recognition and energetic treatment of patients in the earliest phase of the disease are measures of paramount importance.

Inactivation of Insulin

Great variability in the pathological lesions and especially their absence in diabetic cases have led many workers to search for the cause of diabetes outside pancreas and to undertake further researches to that effect. As a result many interesting but scattered observations mostly bearing no relation with each other, have been made. Though they much fall short of a satisfactory explanation of the cause of the disease, they are suggestive of the fact that there are possibly multiple factors at work in producing it.

Some of these observations, which are comparatively of recent date refer to inactivation of Insulin by various agents.

It has been suggested that Insulin does not act upon glucose in tissues when tested in vitro, but that it is very effective in lowering the blood sugar in vivo in depancreatized animals (Nitzesen 1925). It is suggested that Insulin itself is an inactive substance which may be produced in adequate quantities, but that there is some substance (activator) in the body which activates Insulin and enables it to act on glucose and that this activator is absent or deficient in diabetes.

One suggestion according to Himsworth (1933-34) is that such an activator—called Insulin-kinase—is a hormone produced in the liver, it takes some time to activate Insulin thus explaining the time (latent period) that elapses between Insulin injection and the fall of blood sugar. There is not much direct evidence to support this theory.

Kallitz, Cohen and Leader have suggested inactivation of Insulin by an enzyme present in the blood stream. They found that hypoglycaemic action of Insulin in rabbits was impaired by the simultaneous injection of human blood and that when the blood of a diabetic person was injected, it had a more marked inhibitory effect on Insulin than that of a normal person.

De Wenslew and Griffiths detected a substance in the blood of patients apparently of the Insulin-insensitive type, which antagonised the action of Insulin.

Heller, MacCullum and his co-workers (1929-31) found a substance in the extract prepared from the mucous membrane of the duodenum, which when given orally or by injection was found to reduce the alimentary glycosuria of normal or partially pancreatectomized

mized animals This substance which is not yet isolated in a pure state, does not produce any action when the pancreas is totally extirpated It is suggested that this duodenal substance supposed to be very sensitive to the excess of carbohydrate—stimulates the Island cells to secrete Insulin in a way similar to that in which external secretion of the pancreas is produced (MacCullum) In diabetes, there is a failure of this substance to react effectively to the presence of carbohydrate

Epstein's theory Another interesting suggestion is that put forth by Epstein (1925) The antagonism between Insulin and trypsin is well known According to him, trypsin finds through changes in the endothelial permeability, a way into the capillaries, and neutralizes the Insulin secreted into the blood stream Further, when trypsin is carried to the liver, it causes increased glycogenolysis resulting in hyperglycaemia and glycosuria

Defective Absorption of Insulin

There exists a mechanism controlled through either the nervous system or hormones for regulating the output of Insulin in response to demands varying between wide limits It is suggested that this regulation is accomplished by alterations in the amount of blood flow which determines not only the nutrition of the Island cells but also the amount of Insulin entering the blood stream to be distributed to the tissues It is assumed (Warren) that changes occur (f1 spasms, thickening etc) in the blood vessels which interfere with the transport of Insulin - This explains the "emotional glycosurias" as being due to transient spasms of the blood vessels, brought about through adrenals and consequent defective absorption of Insulin in the blood

Another theory is based on alteration of permeability of vascular endothelium (Wiechaman) It is suggested that in diabetes mellitus the endothelium remains permeable to glucose entering the blood stream but is not permeable to glucose leaving the blood vessel Hence there occurs accumulation of sugar in the blood

The Anterior Pituitary Gland and Diabetes

In present days, the question of endocrine glands playing an important role in the causation of diabetes, has greatly come to the forefront and has engaged the attention of a large number of workers Recent researches independently carried out by Houssay in America and Young and Richardson in England, have definitely established the fact of endocrine glands, particularly the anterior pituitary, being concerned more or less in the development of diabetes

The connection between pituitary disturbances and diabetes mellitus has been known long since In 1908 Bouchardt noted that an extract of the posterior pituitary body raised blood sugar level, while in 1911 Cushing observed that pituitary deficiency was attended by an increased tolerance for sugar Glycosuria has frequently been found in

clinical conditions attended by lesions such as growth, haemorrhage etc., in the region of the pituitary. In acromegaly, due to an adenoma of the anterior lobe of the pituitary, hyperglycaemia has often been noted and which disappeared later when the tumour cells passed into a degenerative phase.

Houssay, Evans and several other workers independently have shown that daily administration of extracts of the anterior pituitary gland to normal animals, under suitable conditions, induced the appearance of diabetic symptoms, which however disappeared soon after the daily injections were stopped. Further, Young and Richardson (1938) have been able to produce permanent diabetes in 5 out of 6 dogs by daily injection of certain pituitary extracts for a few days.

The fundamental importance of the discoveries of Houssay and Young lies in showing that normally there must be a balance of action in the body between *anti-diabetogenic factors* (Insulin and Insulin like substance) and *diabetogenic factors* (anterior pituitary and contra insular substances). The effect of an anti-diabetogenic substance (Insulin) is to keep down the blood sugar either by glucose oxidation or glycogenesis (glycogen formation), whilst the diabetogenic substance (anterior pituitary substance) would raise the blood sugar level, and induce the appearance of diabetic symptoms. Anything that affects the normal activity of either of the two, eventually opposing factors, either in the increase or decrease, would disturb the finely adjusted balance of action and would produce either hyperglycaemia or hypoglycaemia depending upon the way and extent to which these diabetogenic and anti-diabetogenic factors are involved.

Thus, it will be seen that diabetes mellitus may in some instances be due not to a deficiency of Insulin but to an excessive secretion of the diabetogenic substance of the anterior pituitary gland. In the latter case, the amount of Insulin secreted by the pancreas might be normal or even abnormally great, but nevertheless, more Insulin would be required to overcome the antagonistic action of the pituitary substance.

By accepting the new theory, the existence of Insulin-resistant cases, becomes easily understood. These cases were a puzzle for a long time because very large doses of Insulin, occasionally many times the amount of Insulin which human pancreas is considered normally to secrete, were necessary to keep the urine from sugar.

Further experimental work has shown that the anterior pituitary body over and above the diabetogenic substance (that which antagonises the action of Insulin) contains another substance (Pancreatotropic hormone) which has an influence on the Island cells of the pancreas. Anselmino and Hoffmann showed that the administration of suitable anterior lobe extracts caused an increase in the amount of the Island tissues in the pancreas and a fall in blood sugar, but results were not sufficiently convincing. However very recently, Richardson and Young (1938) using a method which would permit of determining

the amount of Island tissues, observed in rats proliferative changes in the Island cells of Langerhans, together with an increase more than twice in the amount of Island tissues after daily injection of certain anterior pituitary extracts for a period of about 15 days. These rats were observed not to exhibit symptoms of diabetes as a result of anterior pituitary injections.

On the other hand, they found that in dogs injections of constant but small amounts of anterior pituitary extracts produced at first, diabetic symptoms which later disappeared in spite of the injections being continued. Increase in the dose again was found to be followed by appearance in sugar in the urine, only to disappear a little later. But later, they found that in dogs when comparatively larger doses were given the diabetic symptoms failed to disappear as with the smaller doses after the injections were stopped (Richardson and Young, 1938). The animals thus became permanently diabetic.

The phenomenon of the appearance and disappearance of the symptoms of diabetes following each increase in the daily amount of extract injected is explained on the assumption that the pituitary extract contains two different substances one of which causes the Island cells of Langerhans to grow while the other antagonises the substance. On the other hand in the dog, the diabetogenic substance is more rapidly effective than that stimulating the growth of the Island cells of Langerhans to grow while the other antagonises Insulin. On the other hand in the dog, the diabetogenic substance tissue had sufficiently occurred to provide more Insulin to neutralize the action of the diabetogenic substance.

But when large doses are continued for a long time, the Island cells may be overstrained and may undergo degenerative changes similar to those seen in dogs made permanently diabetic by Richardson and Young.

This work of Richardson and Young gives support to the new theory of anterior pituitary diabetes, as it is shown that if a diabetic condition is produced even for a short time it may lead to secondary changes in the pancreas which may become permanent and may make the diabetic condition to persist indefinitely, even though the abnormal influence of the pituitary gland be removed. If the cause is not removed, the diabetic condition may become worse and worse ("The anterior pituitary gland diabetes"—*Diabetic Jour* Vol II No 14 April, 1938).

Further evidence in support of the anterior pituitary diabetic theory is provided by the following facts (1) Diabetes occurs at an age between 11 and 13 years in the overgrown child (2) Its incidence in women is greater at the time of menopause. At both these periods of life, pituitary gland is known to become hyper-active (3) It occurs in the obese (4) Diabetes is altered by removal of the pituitary (5) It

is known that endocrine functions are controlled by the law of recessive mendelism (Joslin)

The new theory of anterior pituitary diabetes however attractive it may be, does not belittle the importance of the epoch-making discovery of Insulin by Banting, as it does not carry us an inch further in the treatment of diabetes for which at present Insulin is the only one satisfactory method of treatment. It is difficult to apply the results of animal experiments to human diabetes and questions such as "What causes hyper-activity of the anterior pituitary" or rather "What causes imbalance of action between anti-diabetogenic and diabetogenic factors" "How anterior pituitary substance hinders the activity of Insulin", remain yet unsolved and need further investigations.

Other Endocrine Glands and Diabetes

Adrenals and thyroid are known to have some share though a minor one in regulating carbohydrate metabolism and they when diseased or injured may cause diabetes to develop.

Adrenals Glycosuria produced by adrenaline was first noted by Blum. Though clinical cases of adrenal glycosuria are practically unknown, still adrenaline is found readily to produce glycosuria in animals (Britton and Salvette). Prolonged use of adrenaline has been known to produce glycosuria in man. Glycosuria from fear or excitement is considered to result indirectly through the stimulation of adrenaline secretion. The action of Adrenaline (medullary secretion) is thought to be physiologically antagonistic to that of Insulin. It is believed that the adrenaline glands are extremely sensitive to blood sugar levels, a slight fall stimulating more adrenaline secretion which in its turn causes increased glycogenolysis and a rise in blood sugar level. The presence of adrenals is deemed necessary for the action of anterior pituitary in raising blood sugar level.

Cortisin is also found to possess an anti-insulin effect on carbohydrate metabolism, and when it is deficient as in cases of Addison's disease, hypoglycaemia may occasionally be produced.

Thyroid In disturbed states of thyroid it is not uncommon to find glycosuria. In Grave's disease, patients are often found to suffer from hyperglycaemia as well as glycosuria, but severe diabetes in them is rare. On the other hand in myxoedema, sugar tolerance is usually raised. Removal of a large portion of thyroid in a diabetic patient is often followed by amelioration of the diabetic symptoms, and a decrease in the Insulin requirement (Yriat and Wolfson), though this is doubted by some observers. Administration of thyroxin over long periods is often followed by glycosuria, and therefore should be avoided in diabetes.

(To be continued in the next issue)

Critical Notes and Abstracts

CHRONIC HYPERTROPHIC EMPHYSEMA

Ronald V Christie of St Bartholomew's Hospital, London, discusses the etiology and the cause of some of its signs and symptoms. The description of this type of emphysema which is given in most textbooks of medicine includes little that Laennec did not describe in 1819. Numerous hypotheses have been advanced to explain the cause of chronic emphysema, but most are based only on conjecture and are incapable of experimental analysis or proof. Most are agreed that chronic bronchitis or asthma may lead to emphysema. There is no good evidence of any relationship between occupations such as, glass-blowing, the blowing of wind instruments, singing, preaching, crying etc and emphysema. It is a striking testimonial to the conservatism of medical teaching that there is no textbook of medicine which does not quote glass-blowing and the blowing of wind instruments as possible or probable causes of emphysema, and this in spite of ample evidence that no such aetiological relationship exists. The original statement of Laennec has evidently been copied from textbook to textbook over a period of 120 years. There is no good evidence to support the supposition that manual labour, strenuous exercise, residence at high altitudes, changes in the thoracic cage, degenerative changes in the lung and visceral pleura, pulmonary arteritis, arteriosclerosis of the lung, and inflammatory lesions in the lungs are responsible for emphysema. It is probable that some of these factors may cause an increase in thoracic size rather than true emphysema. In the author's experience at least 90 per cent of these patients with symptoms and signs of emphysema have a history of chronic bronchitis or asthma of several years' duration.

It is safe to say that chronic bronchitis and asthma are the only conditions which have been shown to lead to hypertrophic emphysema of the lung. Coughing or breathing against resistance subjects the alveolar walls to abnormal stresses and strains. Sudden pressure changes within the alveoli of 20 to 30 cms of water must result in considerable stresses and strains on the flimsy structure of the alveolar wall. In time the lung will begin to show the signs of wear and tear which we call emphysema, but certain individuals can tolerate these stresses and strains for longer than others, and age is an important factor. The loss of elasticity of the lungs produces the "barrel-shaped chest". The expiration is performed by an unnatural respiratory act, and it becomes an active rather than a passive act and it is probably for this reason that expiration is prolonged in emphysema.

Respiratory distress is a prominent symptom in emphysema. An unnatural inspiratory effort has to be made to inflate the lungs and a large part of the air inspired is wasted on relatively functionless alveoli. Even after this wasted effort the lungs cannot relax passively, but have to be compressed by an unnatural expiratory effort.

The immediate result of this unequal and wasteful distribution of ventilation in the lungs is inefficient aeration of the blood. There is a compensatory rise in the alkali reserve in these patients, and they are not short of breath while at rest, but they become dyspnoeic only when there is a sudden increase in CO_2 production, such as occurs on even mild exercise. Furthermore, they are not orthopnoeic, and this is to be expected as there is no evidence that emphysema in itself leads to pulmonary congestion. It is only if heart failure supervenes that orthopnoea may appear.

The destruction of capillaries in the overstretched and torn alveoli diminishes the pulmonary vascular bed and makes it more difficult for the right ventricle to drive blood through the lungs. Right ventricular hypertrophy might therefore be expected, and it does in fact frequently occur. For the same reasons there is a tendency towards dilatation and hypertrophy of the pulmonary artery. The absence of a negative intrapleural pressure is also an important factor in the circulatory disturbance. Venous blood is no longer sucked into the thorax by the intrapleural pressure as in normal persons, and the pressure in the systemic veins therefore tends to be raised.

Clinicians have for long been aware of so-called right heart failure in emphysema, where the venous pressure is raised, the liver is enlarged, and the dependent parts somewhat oedematous, with little or no evidence of pulmonary congestion. The explanation of this type of heart failure probably lies in these two factors, the destruction of pulmonary capillaries and the altered intrapleural pressure both of which tend to impede the flow of blood through the lungs but in no way embarrass the left ventricle.

THE EFFECTS OF OXYGEN AND CARBONDIOXIDE INHALATION IN CASES OF CORONARY THROMBOSIS

It has been shown, beyond doubt, that the inhalation of high-oxygen atmospheres has a beneficial physiological action on coronary circulation, when the latter has been previously impaired, there is improvement in the function of the coronary circulation. In 1929, Rizer⁶ demonstrated the effectiveness of a 50 per cent oxygen mixture in relieving the precordial pain of coronary thrombosis. More recently (1940), Boland¹ has reported immediate and striking relief of pain in coronary thrombosis by the inhalation of pure oxygen. Barach and Levy¹, discussing the question of oxygen-therapy in the treatment of coronary thrombosis, in 1930, said that a 50 per cent oxygen mixture may prove successful in cases of coronary thrombosis where peripheral failure has supervened, marked relief of symptoms was noted in some of these cases. The effects of inhalation of pure oxygen on the electrocardiogram, both in normal individuals and in subjects of coronary disease were reported by Barach and Steiner² in 1940. Inhalation of pure oxygen in normal persons had no cardiographic effect except in a few who developed increase in height of the T deflection. A similar experiment with subjects of coronary disease,

revealed in many cases an elevation of the T wave, in cases with previously depressed or diphaseic T waves, the latter wave showed a tendency to become upright after the inhalation of pure oxygen

In a more recent paper (1941) Barach and Steiner report the results of further experiments along these lines. The electrocardiographic effects of inhalation of approximately pure oxygen in 32 cases of coronary disease were studied, in 27 cases the T wave was rendered more upright. Addition of carbon dioxide to high-oxygen mixtures had either no effect or a tendency to diminish slightly the T wave elevation subject to oxygen inhalation. On the basis of their experiments and in accordance with the thesis of Macleod⁵ (that the height of the T wave is influenced by the speed of recovery of heart muscle,) Barach and Steiner⁵ have come to the conclusion that inhalation of high-oxygen mixtures in cases of coronary disease, tends to shorten the recovery period of heart-muscle. Inhalations of small amounts of carbon dioxide in these cases have paradoxical effects, in the presence of acute anoxia, carbon dioxide shortens the recovery period of heart muscle, while in the presence of oxygen concentrations, it tends to delay the recovery period of heart muscle.

- (1) Barach A L and Levy R L J A M A 94 1363 (1930)
- (2) Barach A L and Steiner A Proc Soc. Exper Biol & Med 45 175 (1940)
- (3) Barach A L and Steiner A Amer Heart Jour 22 13 (1941)
- (4) Boland E W J A M A 114 1512 (1940)
- (5) Macleod A G Amer Heart Jour 15 165 (1938) *ibid* 15 402 (1938)
- (6) Rizer, R J Minnesota Med 12 506 (1929)

R J VAKIL

ANEURYSMAL DILATATIONS OF THE SINUSES OF VALSALVA

Micks, R H Brit Heart Jour 2 63 (1940)

The subject of aneurysms of the sinuses of Valsalva receives the briefest mention in text-books of medicine. Aneurysms of the aorta involving one or more sinuses of Valsalva have been reported on numerous occasions. They have ascribed in the majority of cases to either syphilis or ulcerative endocarditis; there are however cases on record where no evidence of these two causes could be discovered and they were considered congenital.

Micks' case is unique because it describes aneurysms of all three sinuses of Valsalva, such cases being extremely rare, this author has been able to trace only 3 records of similar cases (Carpentieri's case at Naples, Barnscheidt's case at Bonn, and Haban's case at Budapest). In Micks' case gross aneurysmal dilatations (over 50 cm deep) of all three sinuses of Valsalva were present because of their symmetrical nature, their lining of endothelium and the absence of syphilitic and ulcerative lesion, they were ascribed to a congenital anomaly. The aneurysm of the left sinus of Valsalva was over 60 cc in volume, of the right sinus 15 cc and of the posterior sinus 9 cc in volume. The patient was in perfect health till a short time before death, when he

developed several interesting disturbances of rhythm, he died of acute heart failure and complete heart block. Ante-mortem diagnosis of this condition is impossible in the present state of our knowledge.

R J VAKIL

ELECTROCARDIOGRAPHIC CHANGES IN PELLAGRA

In view of the fact that two interesting papers on Pellagra have appeared in second issue of the *Indian Physician* a consideration of the electrocardiogram in this disease may not be out of place here.

From the clinical point of view, certain circulatory derangements may be observed in cases of pellagra, the most frequent being a rapid pulse, a low blood pressure and oedema.

Porter¹, in 1934, could find no electrocardiographic changes in pellagra except a sinus tachycardia. In 1936, Feil¹, after an electrocardiographic study of 38 cases of pellagra, reported certain characteristic alterations of the electrocardiogram in 14 cases (i.e. 37 per cent). In the limb leads of these electrocardiograms he noted (1) sinus tachycardia, (2) low voltage type of QRS complex, (3) abnormal T waves e.g. high T waves, inverted T waves or the Paidee type of T waves and (4) abnormal S-T intervals. In the chest-leads, he noted low voltage, M shaped QRS complex, etc. With treatment of the pellagroid condition, these alterations were found to retrogress and disappear.

In 1940, Mainzer and Kianse², reinvestigated this problem in 23 pellagrins (with normal circulatory condition).

Abnormal cardiograms were described in as many as 57 per cent (or about three-fifths) of their cases. The most frequent electrocardiographic abnormalities were (1) tachycardia at the height of the disease and bradycardia during convalescence, (2) low voltage and notching of the QRS complexes, (3) shortening of the P-R interval, (4) alterations of the S-T interval and (5) inversion of the T wave.

These alterations have a development parallel to the clinical course of the disease and disappear rapidly after treatment with nicotinic acid, thus proving their casual relationship to Pellagra.

(1) Feil, H. *Amer Heart Jour* 11: 173 (1936).

(2) Mainzer, F. and Krause, M. *Brit Heart Jour* 2: 5 (1940).

(3) Porter, W. B. "Modern Concepts of Cardiovascular Disease", 3: 9 (1934).

R J VAKIL

A STUDY OF 31 CASES OF TUBERCULOUS PERICARDITIS

H. L. Helmann and Binder, *S. Brit Heart Jour* 2: 165 (1940).

Helmann and Binder have reported a careful study of this uncommon clinical manifestation of tuberculosis. They have met with as many as 31 cases of tuberculous pericarditis in their experience of

fifteen years at the Johannesburg Hospital, S Africa Some of their cases were of "primary tuberculous pericarditis" while others belonged to the group of "generalized tuberculaemia" They believe that the condition of tuberculous pericarditis begins acutely, passes into a stage of effusion or caseation and finally goes into the adherent stages This was clearly shown in three of their cases In 9 of their cases, the area of cardiac dullness was normal in size while in 19 cases with a serious, haemorrhagic or caseous exudate in the pericardial sac the area of the cardiac dullness was enormously enlarged with a characteristic "pear-shape" and an "obtuse cardio-hepatic angle"

These authors describe three possible *modes of spread* by which tuberculosis may reach the pericardium (1) spread by direct contact, (2) spread by the bloodstream, and (3) spread by the lymphatic route In their opinion, the glands at the root of the lung are the usual origin and source of spread, while the lymphatics are most often concerned in this spread

Clinical Features Tuberculous pericarditis is much commoner in males than in females (about 3 : 1 in this series), it is commonest between the ages of 20 and 40 years and in coloured races The usual history given by these patients is one of the typical congestive cardiac failure Diagnosis depends on (1) a diagnosis of pericardial disease, with all its signs and (2) on establishing the tuberculous nature of the pericardial disease For the guidance of the reader, Heimann and Binder have given a list of features which, in the presence of pericardial disease, suggest the condition being tuberculous (1) The presence of a chronic wasting disease, (2) Fever, intermittent or remittent, (3) Evidence of active tuberculosis elsewhere (4) congestive cardiac failure with bilateral pleural effusions and without organic murmurs (5) Pericardial fluid, haemorrhagic and containing tubercle bacilli, and (6) the demonstration of a small heart and thickened pericardial wall, on radiography or kymography after pneumo-pericardium

Prognosis The outlook is poor, the patient usually succumbing to military tuberculosis or cardiac failure within one to six months after onset of symptoms

R - J VAKIL

THE ELECTROCARDIOGRAM OF THE STOKES-ADAMS SYNDROME

Parkinson John Papp Cornelio and Evans William Brit Heart Jour 3 171 (1941)

The earliest reference to this condition was not from Stokes or Adams but from Morgagni, who as early as in 1761 described the combination of a slow pulse with syncopal or epileptiform attacks The condition was described more fully by Adams in 1827 and popularized by Stokes in 1846 In 1899, Huchard proposed the term "Stokes-Adams disease", which has persisted ever since

A recent paper by Parkinson Papp and Evans serves to bring together scattered references in the literature regarding the condition

known as Stokes-Adams syndrome. Their paper also includes certain interesting case-records and electrocardiographic studies during the attacks.

According to them, an attack is most likely to occur during the changing of a heart block from partial to complete or during the rapid development of a block but that does not mean that established cases of complete heart block are immune from attacks.

These authors have restricted their study to cases in which an electrocardiogram had been taken during the actual attack (56 reported cases and 8 cases of their own giving a total of 64 cases). The investigation was undertaken with a view to determine the relative frequency and importance of the various disturbances of mechanism responsible for the Stokes-Adams attack. According to the mechanism responsible, they adopt the following classification —

(1) Group I with ventricular standstill alone (33 cases). A feature particularly stressed is that during Stokes-Adams attacks with ventricular standstill the auricle continues to beat while in other forms of cardiac syncope there is, as a rule, a total cardiac standstill.

(2) Group II Ventricular tachycardia followed by ventricular standstill, there may be "low ventricular tachycardia" (i.e. a rate below 160) — (4 cases) or "high ventricular tachycardia" (i.e. a rate between 200 and 500) (14 cases).

(3) Group III High ventricular tachycardia, or ventricular fibrillation or both, without ventricular standstill (13 cases).

(4) Group IV Extreme bradycardia with complete heart block (The authenticity of such case-reports is doubted).

They have come to the conclusion that ventricular standstill is not the only cardiac mechanism responsible for these attacks, it is responsible for about 55 per cent of cases. Ventricular tachycardia followed by standstill accounts for 25 per cent and ventricular tachycardia without subsequent standstill for 20 per cent.

The essential cause of an attack can only be determined by the electrocardiogram. The electrocardiogram is of great significance in prognosis because patients with ventricular standstill (Group I) have a fair chance of recovery and may live for years, while patients in Groups II and III seldom recover and then not for more than one year.

This is undoubtedly the most exhaustive and illuminating paper ever published on the subject of mechanisms underlying the Stokes-Adams attack.

R. J. VAKIL

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Let us remember

CIRCULATION OF BLOOD

By

AMRUT MODY,

M SC (LOND)

BOMBAY

The art of medicine as practised in ancient Greece became fixed as a doctrine not only in the Hippocratic writings but also in the Galenical books. Not until the Renaissance in the 16th century did anyone arise to question the infallibility of Galen or the superabundance of fanciful hypothesis that had entered during the Arabic translations. It was in Arabic guise that Greek medicine was introduced to Western Europe.

Galen's views on the heart and the blood vessels were briefly as follows. Blood is formed, and endowed with "natural spirits," in the liver, whence it flows through the veins to the various parts of the body and returns again by the same veins to the liver—the movement being rather like a tidal ebb and flow. The right ventricle of the heart is a part of the venous system. Of the blood which enters it, after discharging its impurities into the lungs, the major portion returns to the liver, while the rest penetrates the porous wall (or septum) and enters the left ventricle, where it mingles with the air coming from the lungs, and is converted into a kind of more refined substance called "Vital Spirits." These vital spirits are conveyed by the arteries to various parts of the body, including the brain. The vital spirits which enter the brain are there refined into "animal spirits," which the nerves (conceived as hollow tubes) distribute all over the body. The uncertain semi-material and semi-spiritual status of the various "spirits" were a doubtful help to doctors in perplexity, and a positive hindrance to the advancement of medical science and practice.

The great divide between the old medicine and the new, the event which seemed almost to close the Arabic epoch, was the publication at Basel in 1543 of the famous book "*Fabrica Humani Corporis*" by Andreas Vesalius (1514-64). His methods and his instruments were new and epoch making. He ended the long reign of fourteen centuries of precedent and authority.

Among the numerous errors of Galen which Vesalius corrected, we are specially interested in his views on the structure of the heart. According to Galen, as has already been stated above, the septum or wall between the two ventricles of the heart is porous, so that some of the blood can percolate through it from the right to the left ventricle. This idea was definitely rejected by Vesalius in the following words: "It seems to me that the septum of the heart is as thick, dense and compact as is the rest of the heart. So I do not see how even the smallest particle can pass from the right to the left ventricle through the septum." Moreover, his sketch of the portal circulation shows such a close mutual approach of the minute terminals of the arteries and of the veins in the tissues of the body, and his account of the portal vein and the vena cava states so clearly that "the extreme ramifications of these veins inosculate with each other, and in many places appear to unite and be continuous," that one wonders how he failed to conjecture that the blood circulates. However, he did fail, and the next step towards the recognition of the circulation of the blood was taken by Servetus.

Michael Servetus (1511-53) a Spaniard, but a co-student of Vesalius at Paris gave a further lead by the publication of his book on "Restitution of Christianity." The passage important to us for the present reads as follows —

"In order that we may understand how the blood is the very life, we must first learn the generation in substance of the vital spirit, which is composed of, and is nourished by, the inspired air and the very fine blood. The vital spirit has its origin in the left ventricle of the heart, the lungs especially helping towards its perfection, it is a thin spirit elaborated by the power of heat, is of a light colour, of a fiery potency. It is generated through the co-mingling, in the lungs, of the inspired air with the elaborated fine blood communicated from the right ventricle to the left. This communication does not take place through the septum of the heart, as is generally believed, but a special device drives the fine blood from the right ventricle through a long passage in the lungs. There it is rendered lighter in colour, and from the pulmonary artery is poured into the pulmonary vein. Here it is mixed with the inspired air, and by expiration is cleansed of its fumes. At length, completely mingled with the air, it is drawn in by the left ventricle during its dilation, and is fit to be vital spirit."

A further step in the right direction was the publication by Hieronymus Fabricius (1537-1619) of a booklet "on the Valves of the Veins." When the arm is bandaged above the elbow the veins swell up which was explained by him on the ground that the thin little membrane on the inside of the veins opened towards the heart but closed in the opposite direction.

The story was completed by Harvey. The discovery of circulation of blood was announced by him at the college of physician in London in 1616 and published in his book "De Motu Cordis" at

Frankfort in 1628 But this important discovery was the climax of the study of the work of Vesalius, Servitus, Realdus, Columbus, Fabricius and others When Harvey went to Padua and sat at the feet of old Fabricius in 1600 much was known about the heart and the blood He there listened to Fabricius and then studied the matter for himself in man and animals

"I profess," he says, "to learn and to teach anatomy, not from books, but from dissections, not from the positions of philosophers, but from the fabric of nature"

Harvey's conception is the modern conception of the circulation of the blood and needs no elaboration The great tribute to Harvey is in fact a tribute to the struggle waged by the inquiring spirits of the renaissance to free the biological sciences from the obscurantism which haunted them so long as quasi-spiritual categories, instead of physical and chemical categories, were used in the explanation of the phenomena of life

The final touches were given by Marcello Malpighi (1628-94) who not only made the full use of the microscope, a toy at that time recently invented but also introduced the method of injecting water into arteries, thus washing the blood from the vascular system and making the blood vessels more visible It was his study of the lung of the frog that led him to the discovery that the lung is not, as used to be supposed, a homogeneous tissue in which the air and the blood mingle, but that it contains air cells, and that a membrane always separates the blood from the air so that they cannot come into immediate contact in the lungs In 1660, while pursuing these investigations, Malpighi first saw the blood pass through the capillaries embedded in the lung of the frog and connecting the arteries with the veins Later on he discovered capillaries also in other parts of the body

The progress in the development of the idea of circulation of blood makes an interesting reading It shows the effect of the epoch as well of the interrelation of studies of several great men

Original Contributions

BANTI'S SYNDROME

By

V S PURANDARE

M B B S

BOMBAY

In the every day practice, one rarely sees cases of Banti's Syndrome and hence one may miss the condition unless kept in mind. Recently a case of Banti's Syndrome was admitted in the J J Hospital, Bombay, an account of which, with a brief review of the disease, is presented here.

History of the case A boy aged 17 years was admitted in the J J Hospital for hæmatemesis which had occurred at frequent intervals. Last attack had occurred on the 22nd Oct 1941. The patient also had enlargement of the abdomen for the last two years, and fever with rigors for six months before the beginning of the enlargement of the abdomen. On examination his spleen was found to be greatly enlarged, reaching nearly as low as the umbilicus, the edge of the liver was felt below the right costal margin. There was free fluid in the abdomen.

Stools, urine and ascitic fluid showed nothing abnormal on usual investigations. The examination of the blood showed hæmoglobin 32%, red blood cells 2,000,000 per cmm, colour index 0.8, white blood cells 4,200 per cmm.

Van Den Bergh Reaction—Delayed Direct Positive. Icteric Index 15. Two more blood examinations were done but the blood as well as the Van Den Bergh reaction did not show much difference.

Surgeon's Notes There were not many adhesions round about the spleen and no abnormal hæmorrhage occurred at operation. Liver was enlarged and on the inferior border hard red nodules were visible. In general it looked cirrhotic.

Spleen Naked eye appearance. The size of the spleen was 20 by 15 cms, it was firm in consistence, the weight of the spleen was 1050 grammes. Colour of the spleen was dark grey.

and its cut surface had a fibrous appearance and showed a number of yellowish granular areas uniformly scattered all over its surface. Trabeculae were well marked and the spleen pulp appeared reduced in size. On sectioning no blood escaped from the spleen.

Histology A section of the spleen stained by haemotaxin and eosin showed a number of nodules in various stages of formation. In some nodules surrounding the central artery, there were young foamy cells, a zone of immature connective tissue, then a zone of giant cells and fibrous tissue. In others which represented further stages of formation, there were areas with elongated and special cells containing some blackish and yellowish pigments and surrounding this, a zone of well formed fibrous tissue followed by a zone of mononuclears. These elongated and branching pigment cells have frequently in the past been interpreted as finer mycetæ but it is found that this view is based on insecure evidence and it is shown by special staining that the pigments are derived from the breaking down of Hæmoglobin. These nodules are the same which are known as Siderotic Nodules or Grand Gamva Nodules.

The trabeculae did not show any abnormality. The Sinusoids were reduced owing to fibrosis. Some Malpighian bodies were normal and some were partially replaced by general fibrosis similar to that found in nodules.

Discussion Splenic anaemia was first described by Gretzl in 1886, but Guido Banti, in 1883 first gave a systematic description of the spleen. Later on he described a characteristic symptom-complex, which has since been known as Banti's Syndrome. He divided the illness into three stages (1) Preascitic, (2) Intermediary, and (3) Ascitic stage. Preascitic stage is now usually known as Splenic Anaemia. In this stage there is an enlargement of the spleen usually very great and an anaemia with leucopenia. Red blood cells varying between 3 to 4 million per cmm and hæmoglobin is very low, so that the colour index is about 0.5. White blood cells are not increased but often there is leucopenia. The liver may be enlarged at the end of this stage. This stage usually lasts 3 to 5 years but may be prolonged upto 12 years.

Intermediary Stage This stage usually lasts for some months, but sometimes longer. Gastro-intestinal disturbances

set in and there may be severe and repeated hæmatemesis. The liver enlarges but the spleen remains of the same size.

Ascitic stage After sometime free fluid appears in the peritoneum while the liver decreases in size and recedes behind costal margin. Anaemia becomes pronounced and death as a rule occurs within six months after the appearance of the ascitis. Banti held that as a rule the disease is indistinguishable from portal cirrhosis at this stage. He described pathological changes in the spleen as constant and characteristic and claimed to have excluded all other causes of splenic anaemia. But this is disputed by others and the view that has gathered much force is, that the so called Banti's Disease or Splenic Anæmia is but a clinical syndrome which may have different causes.

Etiology The etiology of the condition is still debated and there is a growing disbelief in the conception that this syndrome is a separate clinical or pathological entity. The following facts are given in favour of the above statement. The anaemia is a hypochromic microcytic anaemia and responds to iron therapy. It differs from idiopathic microcytic anaemia and anaemia of malnutrition only in that there is more frequently a leucopenia in this condition. There is nothing in the blood picture to show that the destruction of red blood cells in the spleen is an etiological factor. Similarly changes in the spleen are in no way peculiar or specific. The same changes can be expected in chronic passive congestion. In many of these cases, even when there is no clinical incidence of Liver Disease, tissues removed at operation or autopsy show early or advanced cirrhotic changes. According to Graham Bryce, the clinical and pathological changes of Banti's Disease may be reproduced by several other diseases, particularly by Thrombophlebitis of the portal and splenic veins. Evidence is accumulating for the view that this anæmia is due to the vascular disturbances in the spleen caused by an obstruction in the portal circulation. The anæmia is caused by either iron deficiency or repeated hæmorrhages or indigestion or a combination of these factors.

A few words about the blood picture in this condition will not be out of place.

This is a dyshaemopoietic anaemia with a moderate degree of anisocytosis, microcytosis and hypochromasia. Blood pictures in Banti's syndrome as described by different workers go to prove the above statement.

Chaney² worked out the blood picture of 69 cases of Banti's Disease and gave these as average figures Red blood cells 3 7 million per cmm, Hb 53%, C I 0 72, white blood cells 4900 per cmm

Hanrahen reported on 39 cases His figures are red blood cells 3 3 million, Hb 51%, C I 0 74, white blood cells 4 700 per cmm

Larrabee worked out 47 cases of Banti's Disease His average figures were red blood cells 3 1 million, Hb 50%, C I 0 8, white blood cells 4,600 per cmm

Platelet count may be normal or slightly decreased

Rosenthal has carried out platelet count of such cases and has described two types of cases In one, the thrombocytopenic type, the platelet count is very low and these patients have a marked tendency to hæmorrhage In the other type, the thrombocytæmic group, the count is normal or only slightly subnormal Many of the patients belonging to this group die of portal thrombosis after operation

For the consideration of the evolution of the splenic changes in Banti's Disease, the following characters of splenic circulation should be borne in mind

The splenic artery in man is remarkable for its size in proportion to the bulk of the organ As a rule it is a single vessel, breaking up close to the hilum into a number of branches These finally bifurcate in two delicate arterioles called *Panicilli* These end in ellipsoids which consist of swellings or condensations of lymphoid tissue surrounding the *Panicilli* They act as potential valves preventing all flow of blood backwards from the venous to the arterial side of the spleen This valve action of the ellipsoids and the stasis in the *panicilla* arteries is taken by some workers as an important factor in the production of the histological changes of the Banti's Disease, which are described by MacMichael⁴ to be of the following varieties

- 1 Siderotic Nodules,
- 2 Periarterial Hæmorrhages,
- 3 Periarterial Fibrosis,
- 4 Perimalpighian Fibrosis, and
- 5 Dilated Venous Sinuses

Siderotic Nodules These are often visible to the naked eye. Microscopically there is a central artery with a diameter of 0.1 to 0.5 mm. They are caused by hæmorrhage at the point of termination of the arterioles in the ellipsoids where the valvular arrangement may cause rupture and hence result in hæmorrhage. In the neighbourhood of this artery there is a zone of hyaline connective tissue, the interstices of which contain masses of golden yellow, or pale yellow pigment. Outside this pigmented area there is always a zone of hæmorrhage. McMichael further points out that the periarteriolar changes though of less importance, constantly accompany the Siderotic Nodules.

Periarterial Haemorrhages are usually around small arteries and the diameter of these hæmorrhages is from 3 to 10 times that of the artery. Perimalpighian hæmorrhage often occurs round the small arteries when they curve backwards to end in a Perimalpighian zone, they are just similar to the Periarterial hæmorrhages. Later the concentric connective tissue becomes fibrous and thus the stage called perimalpighian fibrosis develops.

The histological changes found in my case described above, appear to resemble the histological picture in the Banti's syndrome, in its various stages of the formation of siderotic nodules and perimalpighian fibrosis.

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THE SPLEEN IN BANTI'S SYNDROME

By

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The spleen with siderotic nodules described by Dr Purandare is a comparatively rare type of spleen in Banti's syndrome. The diffuse type of fibrosis with enlargement of the spleen is much more common. Within the last year three such spleens were met with by me which are described below. Of these, two were obtained in the autopsy material and one was removed by operation.

The operation case (No 601/41) was a male aged 14, who had an enlarged abdomen since childhood. The enlargement was on the left side until two years back, when the patient had a chronic irregular fever with rigors after which the whole abdomen swelled up, presumably due to ascitis. At the time of admission he also had a capute medusae. There was no hæmatemesis. At the time of splenectomy a distinct uniform enlargement of the liver was noticed. Blood picture was not studied, the patient made an uneventful recovery from operation. There was no follow up.

The spleen was regularly enlarged and weighed 2.5 kgs. Capsule was thickened and there were a few omental adhesions. The spleen was firm and rubbery in consistency. Cut surface was chocolate coloured and there were excessive trabecular fibrous bands.

The other spleen was from an autopsy case (No 432, 15-6-40), a female, age 45, who was treated first for anæmia three years ago, and who recently developed ascitis and hæmatemesis and died. At the autopsy the liver was found to be shrunken, nodular and of a dull yellow colour. The spleen weighing 4 kgm was uniformly enlarged. The capsule was thickened and rubbery to feel. Cut surface was dark chocolate coloured and there were excessive trabecular bands.

The third was a recent case (PM 189 Vol 31) of a male, age 32 who was ailing for some months and died in a train on his way home. A terminal lobar pneumonia on the left side was the cause of death. The spleen was greatly enlarged weighing 4.5 kgm tense and purplish chocolate on cut surface. Liver pale white, mottled, finely granular and enlarged (weight 3.5 kgm). Bone marrow red and hyperæmic. Investigations for malaria, kalaazar and leukaemia were negative.

In addition to these recent cases which could be studied in detail a number of cases of splenomegaly with cirrhosis of the

liver and ascitis with occasionally mentioned anæmia or hæmatemesis were found in autopsy records. Microscopic examination of the spleens had shown the absence of other causative factors. These cases can also be included under the heading of Banti's syndrome.

Among recent 800 consecutive cases of splenomegaly found in the autopsy room, 64 cases could be considered to belong to this group. The splenomegaly was mainly decided by the increase in weight. The increase in weight showed one peculiarity. In cases of enlargement of the spleen in acute infective fevers, the increase in weight was much greater than the apparant size of the spleen suggested. A slight or moderate visible increase in size, was often accompanied by an increase in weight upto 700 gms. In chronic conditions, such an increase in weight was associated with a marked enlargement, the spleen reaching almost upto the umbilicus.

These 64 cases of splenomegaly with cirrhosis of the liver were analysed further. The symptomatology was not available in detail. Anæmia was mentioned in 6 cases only. Ascitis to a marked extent was present in 48 cases. There was a terminal pneumonia in a very large number of cases, 38 out of the 64. Hæmatemesis were mentioned in 9. The age distribution was rather peculiar. Only 15 were beyond the age of forty and in this group the liver was atrophic in 11 only, granular in 2, and enlarged in 2 cases. The extent of splenic enlargement was moderate. Ascitis was only present with atrophic livers. In twelve cases the weights were between 500 to 700 gms. In only three cases was the weight beyond 700 gms. And even then the maximum weight was 1200 gms. In the 49 cases below the age of forty, 34 were between the age of 18 to 28 and the rest of higher age. The liver was atrophic in 18, hypertrophic granular in 29 and only enlarged in 2 cases. Ascitis was present in 37 cases, and was present with both atrophic as well as hypertrophic livers. Jaundice which is so commonly present in cases of infantile cirrhosis was not noticed in any of these cases. The enlargement of the spleen was very great in this group. Only 10 spleens weighed upto 700 gms. The rest weighed more than 1500 gms and usually ranged between 1500 to 2500 gms. The maximum weight being 3200 gms. The condition of the spleen was more or less constant. The spleen was firm, rubbery to feel and showed few adhesions. There was a thickening of the capsule but cartilaginous patches of perisplenitis were not men-

tioned Cut surface showed excessive fibrous tissue and firm dark chocolate coloured pulp White coloured irregular patches, which might be siderotic nodules, were described in one, and infarct like areas in another

Thrombosis of splenic radicals or any varicose condition of the spleen was not noticed nor was there any note on the condition of the main portal vein or its radicals in the liver substance

In a few occasionally noticed cases of chronic portal thrombosis or sclerosis, there has not occurred any siderosis or marked enlargement of the spleen

Attempt was made to find out if there was any similarity between the splenomegaly with cirrhosis and a primary infantile cirrhosis Splenomegaly was not a constant accompaniment of this condition But of the eight cases observed in the autopsy room the spleen weighed more than 500 gms in three cases only and the weights were only upto 750 gms The ages of the cases were beyond fourteen in all, and so a weight of this kind could not be considered to be proportionately greater

Histologically, the spleens of the infantile cirrhosis cases tended to show a focal degenerative and hæmorrhagic collection more commonly than the spleens of the general group Bluish staining fibres in groups and hyaline change and proliferation in trabecular areas, were also more marked The pulp usually showed a marked engorgement but very little hyperplasia of intersinusoidal cells

The spleens of the general group showed on microscopic examination, a diffuse proliferation of intersinusoidal cells, an atrophy of malpighian bodies and scattered brown and golden pigment derived from hæmolysis Long fibroblast like cells, containing bluish coloured pigment, or giant cells were not present

The detailed histological studies of the recent cases showed the following appearance

In No 432 the trabeculae showed maximum changes chiefly consisting of new perivascular fibrosis and deposition of reddish brown pigment in strands There were no cellular collections around these pigment deposits under high power The pigment

This mechanism is fairly well illustrated by the present case with siderotic nodules, but does not offer any clear explanation of the changes found in the majority of splenomegalies where there was only a diffuse change

Summary

A series of cases of splenomegaly and cirrhosis of the liver have been discussed. In only one case siderotic nodules with typical histology were found. In all others a diffuse proliferation of intersinusoidal endothelial cells was the constant change.

The age distribution was peculiar. The greater number of cases was found in earlier age groups. Enormous spleens with hypertrophic or interlobular cirrhosis were predominant and found in the age group 18 to 28. Beyond the age of 40 atrophic cirrhosis and moderate splenomegaly were common. The number of cases in this group was comparatively small.

Primary changes in the spleen, rather than in the liver seem to be responsible for this condition but the exact mechanism could not be defined by the present study.

CARBON-MONOXIDE POISONING

A REPORT OF 6 CASES

By

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Going through the annual reports of the Chemical analysers of the various industrial towns and cities one finds that more deaths are caused by carbon-monoxide than any other poison. In our city of Bombay we find several cases of carbon-monoxide poisoning every year. Most of these cases are accidental, a few are suicidal and hardly any are homicidal. The relative percentage of suicidal cases is more in the Western countries than in India.

Carbon-monoxide is an odourless, colourless, and tasteless gas, burning with a blue flame and almost insoluble in water and alcohol. It is found wherever there is burning of carbon with an insufficient supply of oxygen and is consequently very widely met with in the modern economic state of our lives.

Source

In domestic life charcoal fires, "Sigrees", certain types of slow-combustion stoves and water heaters are common sources of carbon-monoxide and give rise to poisoning in the absence of adequate ventilating flues. The exhaust fumes from motor-cars and petrol burning engines contain considerable amount of carbon-monoxide and when inhaled continuously over long periods they may give rise to chronic carbon-monoxide poisoning. The commonest source is coal gas used for heating and lighting purposes. In industrial life the common sources of carbon-monoxide are coal mines, blast furnaces, gas engines, soldering and welding processes and manufacture of water gas, producer gas and coal gas.

Pathology

The limit of toxicity of carbon-monoxide in air is 0.02% but symptoms have been known to have occurred with the lowest concentration of 0.01% Carbon-monoxide in air. A concentra-

tion of 0.07% carbon-monoxide in air is potentially lethal and a concentration of 0.1% is a definite danger to life

The affinity of hæmoglobin for carbon-monoxide is 220 to 300 times that of oxygen hence if an atmosphere containing appreciable quantity of carbon-monoxide is inhaled the oxygen is displaced from the hæmoglobin and the effects of anoxæmia are manifested. But physical displacement of oxygen is not the only mode of action of carbon-monoxide. Carbon-Monoxide itself is a tissue poison and though the nervous tissue is the one which is most susceptible to it, other tissues, and especially the cardiac musculature are known to be affected by it. The fact that carbon-monoxide is a tissue poison is proved from the observation that 50% saturation of hæmoglobin with carbon-monoxide results in much greater asthenia and leaves behind more permanent damage than when a healthy person loses 50% of his hæmoglobin in an equal time.

When death occurs as a result of acute carbon-monoxide poisoning the post-mortem appearance is very characteristic. The skin and conjunctivæ are of a pinkish colour and if the body has remained for some time after death the areas of hypostatic congestion are also pinkish in colour in contrast to the usual post-mortem lividity. The blood remains fluid and does not clot easily even on shedding. The blood in the veins, capillaries and the arteries is of a uniform cherry-red colour and there is absence of post-mortem clotting. All the viscera are of a red colour and congested and œdematous. Lungs may be frothy and there are petechial spots on the pleura and the pericardium. Uncommonly red hæmorrhagic patches may be found symmetrically distributed on the extremities or along the course of the bigger nerve trunks.

In the nervous system, cells of the grey matter show degenerative changes and there may be bilateral softening of pallidial part of the lenticular nuclei which is thrombotic in origin.

In cases dying of Carbon-monoxide poisoning the putrefactive changes are delayed and carbon-monoxide was detected in blood spectrophotically and chemically two and seven months after death by Auteuier and Lagun respectively. On the other hand Mathur of Lucknow is of opinion that in rats dying of carbon-monoxide poisoning the organs begin to decompose on the third day and the blood on the fourth day. Newcomb has

observed that in cases dying of carbon-monoxide poisoning small pieces of tissue taken for microscopic examination do not lose their cherry red colour for 48 hours and even longer in formol-saline and the supernatant fluid remains quite clear

Clinical Manifestations

The clinical manifestations are so varied that they present a collection of signs and symptoms which may be almost negligible or may result in rapid death depending upon the concentration of carbon-monoxide in blood and the time taken to attain that concentration. The six cases reported in this article are selected with a view to bring out these different clinical pictures

Case 1 A male aged 32, a fireman, was admitted to the hospital in a slightly dazed condition. He gave history of having lost consciousness for a few minutes while working a water hose on a smouldering building. He was removed from the scene of fainting and regained consciousness after about 10 minutes.

On admission he complained of a severe headache. The conjunctiva were red in colour and the nails were cherry red. No other physical signs were detected on a routine examination.

Blood showed bands of carboxyhaemoglobin on spectroscopic examination.

The patient was discharged after three days, relieved of his headache by symptomatic treatment.

Case 2 G.R., a male aged 22, a sewer cleaner had gone down a man-hole for cleaning it. After 30 minutes he complained of giddiness and was immediately hauled up. When he was brought to the surface he was unconscious. Within 10 minutes he regained consciousness but still complained of giddiness and a sensation of dragging in the stomach. When brought to the hospital his mind was clear, he narrated the incident correctly and answered questions promptly.

On examination the mucosa of tongue, the conjunctiva, and the nails were found to be red in colour. His temperature was 98° F pulse rate 108 and respiration 32 per minute. The blood pressure was 125 mm of mercury systolic and 80 mm of mercury diastolic. All the tendon reflexes were brisk, there was no ankle or patellar clonus and the planter response was flexor on both sides. No other abnormal physical findings were noted.

Laboratory Investigations

Red blood cells 4.4 million per cmm. Haemoglobin 80%.

Spectroscopic examination of the blood showed presence of Carboxyhaemoglobin bands. The chemical test for carboxyhaemoglobin was not done.

Urine showed a trace of albumen and occasional granular casts with plenty of amorphous phosphates

The patient was given 5% carbondioxide with oxygen and treated symptomatically for his headache

After 8 hours the blood was again examined for presence of carboxaemoglobin by spectroscopic method but its presence could not be detected. The oxygen-carbondioxide inhalation was there after stopped. The cherry-red colour of nails had also cleared. He still complained of a feeling of heaviness in the head 3 days after the accident and was treated with coal-tar analgesics. He was discharged, symptom free, after a stay of nine days in the hospital.

Case 3 On the night of 16th of October a christian family of seven went to sleep with the door and windows of their room closed and left a partially burning Sigree in the room, after putting some water on the coal, hoping that the fire would be put out in a short time. As the members of the family failed to come out at the usual hour the next morning the relatives forced the door open. They found that four persons had died in the room and a boy aged 14 and two girls aged 20 and 9 (cases IV and V reported below) were in an unconscious state. They were removed to the hospital. On admission the boy had regained consciousness, was feeling very weak and was unable to move his limbs. He was perspiring profusely and was in a dazed condition. He answered questions very slowly, though correctly, and was inclined to drop off to sleep. His conjunctiva was injected, tongue and nails and mucosa of palate were cherry red. The pupils were dilated but reacted well to light and accommodation.

An examination of nervous system showed an extensor planter response on the right side while the planter response on the left side was extensor on the medical aspect of the foot and flexor on the lateral aspect of the foot. His blood pressure was 90 mm of mercury systolic and 58 mm of mercury diastolic. The rest of the systems were normal.

Red blood cell 4.5 million per cmm. Haemoglobin 88%. The urine showed no abnormality.

Spectroscopic examination failed to reveal bands of Carboxyhaemoglobin. The patient was given continuous oxygen and 5% carbon dioxide inhalation, 24 hours after admission, as the cherry red colour of the nails had not disappeared and the respirations were shallow. Within the next 24 hours the red colour of the nails disappeared, the respirations became normal and the planter response flexor. The mind cleared, there was no dizziness or headache and the patient made an uneventful recovery and was discharged after 8 days.

Case 4 A girl, aged 9, a member of the family mentioned above was brought to the hospital in a semiconscious state. Her mind was wandering, she was not able to answer questions and was laughing or crying without adequate reason. On examination of the nervous system she was found to have photophobia, pupils were dilated and contracting sluggishly. There was a bilateral planter extensor res-

ponse and the knee jerks were brisk. The other reflexes were normal. The nails were cherry red and her blood pressure was 90 mm of mercury systolic and 60 mm of mercury diastolic.

Red blood cells 4.2 million per cmm. Haemoglobin 78%. The urine showed no abnormality.

Spectroscopic examination failed to reveal presence of carboxyhaemoglobin. The patient was treated on lines similar to case 3 and made an uneventful recovery.

Case 5. A female, aged 20, of the above mentioned family, was admitted to the hospital in a semiconscious state. She had vomited twice before admission and vomited food material once in the ward.

She could not answer questions, was lethargic and passed stool and urine in bed. Her temperature was 97.8° F, pulse 100 per minute and respiration 38 per minute and very shallow. The nails were bluish and not cherry red. The pupils were dilated, reacted well to light, the deep jerks were normal and the planter response was flexor. Her blood pressure was 98 mm of mercury systolic and 68 mm of mercury diastolic.

Red blood cells 3.8 million, per cmm. Haemoglobin 70%. Urine showed no abnormality.

Spectroscopic examination of blood failed to show carboxyhaemoglobin. The patient was given treatment of collapse and given artificial respiration in the iron lung. She came round after half an hour but she had no idea of what had happened to her the night before. She could not recognise her relatives till the next morning. After that she could remember things and made an uneventful recovery.

Note —Though no bands of carboxyhaemoglobin were detected in the cases 3, 4 and 5 the history and the clinical findings suggested a diagnosis of carbon monoxide poisoning. The post-mortem examination performed on the remaining four members of the family who had died also showed evidence of carbon monoxide poisoning.

Case 6. A male, aged 26, a domestic servant was taking his bath when he suddenly gave a cry and fell down. By his side was a burning Sigree. He was brought to the hospital in an unconscious state. No marks of external injury could be detected on his person. The nails and conjunctiva were normal, the tongue was clean and moist. His temperature was 97 F, pulse 120 per minute and respiration 26 per minute. On examination of the nervous system there was no rigidity of the neck, or limbs, the pupils were equal and contracting well and all the reflexes were normal. Nothing abnormal was detected on the usual physical examination. On the evening of admission his temperature shot up to 100 F, pulse 120 per minute and respirations 28 per minute.

White blood cells 10,300 per mm. Polymorphs 87%, Lymphocytes 11%, Large Mono 2%, no malarial parasites seen in the smear.

CSF Hazy, 58 cells polymorphs predominating, a fair number of red blood cells, proteins increased to 0.1%, globulin slightly increased and sugar normal. No organisms were seen in a smear and none grown on culturing the material. The patient kept up a continuous temperature thereafter ranging between 100 and 102 F. He was treated with quinine by injection, and sulphapyridine besides the symptomatic treatment but did not regain consciousness and died on the 6th day after admission.

A post-mortem examination was held on the body of the deceased and following findings were noted. Eyes deeply congested, blood clots in the pericardium, enlarged pink coloured and haemorrhagic liver, and scattered punctate haemorrhages in the brain substance and the meninges. There was no evidence of traumatic intracerebral haemorrhage. Bands of carboxyhaemoglobin were detected by spectroscopic method while the chemical test was negative. A post-mortem diagnosis of delayed carbon-monoxide poisoning was given.

From the study of the above six selected cases one can see how varied is the clinical picture depending upon the concentration of carbon-monoxide in blood. Working upon himself Professor Haldane has found out the relation of carbon-monoxide concentration of haemoglobin and the symptoms. The first symptoms do not appear till the haemoglobin saturation has reached 20%. At that stage the patient experiences slight headache and a varying degree of lassitude and shortness of breath on exertion. When the concentration reaches 30% the patient suffers from severe headache, nausea, giddiness, tinnitus, palpitations and dyspnoea even at rest. When the concentration rises to 40% there is mental confusion, loss of memory, and inco-ordination of movements and inability to move the limbs. Rarely there may be albuminuria 16% (Leschke) and glycosuria and 8% (Leschke) and blisters on hands and feet have also been known to occur. When the concentration gets past the 50% mark the bliss of unconsciousness supervenes and there may be convulsions of epileptiform nature. Death occurs at 75 to 80% of haemoglobin saturation with carbon monoxide. These percentages hold true if the rise of concentration is fairly rapid whilst with a slow rising concentration all the symptoms occur at lower concentration, death having been known to occur between 50 to 60% haemoglobin concentration because of prolonged cerebral anæmia and destruction of the highly sensitive cells of the central nervous system and of the cardiac musculature. The rate of absorption is greater the younger the individual, i.e., the greater the metabolic rate.

If immediate death does not take place the patient enters the dangerous zone of convalescence. The symptoms of carbon monoxide poisoning are headache, peripheral neuritis in lower extremities, sensory paralysis preceding the motor, retrograde amnesia, melancholia, mania, chorea, parkinsonism, aphasia, encephalitis, optic neuritis, amaurosis, cerebral haemorrhage and dementia. All these changes may be either of a temporary or a permanent nature. Wollek describes a case of a boy of 15 who had temporary amaurosis for 15 days after carbon monoxide poisoning.

Delayed Poisoning

It has been noticed that persons who have apparently recovered from the effects of slight carbon-monoxide poisoning very quickly, sometimes show delayed symptoms suggesting the affection of the central nervous system. They may show the hyperkinetic thalamic syndrome with the peculiar thalamic pains which are resistant to ordinary analgesics or they may show the akinetic striatal syndrome resembling Parkinsonism. These persons show areas of cerebral softening and porous degeneration, of thrombotic origin, on post mortem examinations. The lesions may be unilateral or bilateral.

Chronic Poisoning

In cases of chronic poisoning at least 5 to 8% of haemoglobin concentration is necessary before the symptoms can appear. The symptoms are those of slow cerebral anaemia viz neuræsthenia, headache, nausea, lassitude, lack of concentration and giddiness first noticed on looking upwards. The blood shows a picture of secondary anaemia with lymphocytosis.

To detect the small percentage of carboxyhaemoglobin in blood the ordinary spectroscope is useless and Professor Hart-ridge's Reversion Spectroscope is required.

Treatment

The essential principles of treatment are removal from the contaminated atmosphere, supply of warmth by hot water bags or electric cradle, promoting the circulation by 0.5 to 1 cc of adrenalin subcutaneously and 5 cc of 25% Coramine intravenously, and artificial respiration if necessary. To drive out the carbon monoxide which is already in the blood a continuous in-

halation of 5% carbon dioxide with 95% oxygen is without an equal. It stimulates the respiratory centre, deepens respirations, eliminates carbon-monoxide and helps in the absorption of oxygen.

Conclusion

Carbon-monoxide poisoning cases are not very rare. The symptoms vary considerably and the history is an important aid to diagnosis.

In cases of chronic poisoning the diagnosis becomes very difficult unless thought of.

The treatment if given early produces good results.

(Our thanks are due to the Dean, K. E. M. Hospital and our chief, Dr. N. D. Patel for suggesting this review and for permitting us to report these cases from his wards.)

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Case Reports

A CASE OF FEVER WITH RASH & TROPICAL TYPHUS

By

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BOMBAY

Dr P left Bombay on the 1st of March for Bahrampur in Central India and reached there on the morning of the 2nd March. In his second class compartment there were some Indian Officers who had returned from the theatre of war in the Far East.

On the 5th of March, he left with his father, also a doctor, on a shooting trip in the jungle. Next day, that is, on the 6th afternoon he felt chilly, and considerable malaise, which were neglected. In the evening he developed fever with rigor which rose upto 104°F and lasted the whole night. The fever subsided in the morning (99°F), but came on every day, regularly, with two or more rigors a day. He took quinine hydrochloride gr xxx per day, for the first three days, but as it had no effect he took injections of quinine bihydrochloride gr x for two days but without any effect on the fever.

On the third day, i.e., on the 8th, a morbilliform rash appeared on the forearms, legs, abdomen and the back. There were a few papules in the beginning but more papules appeared on the 6th day of the illness, all over the body.

As the fever would not subside in spite of the quinine by mouth and by injections and as there were repeated rigors daily the patient did not want to stay at Bahrampur and returned to Bombay on the 12th March. I saw him on the same day, i.e., on the 7th day of illness. The temperature was 102.6°F pulse rate 96 per minute and respiration 28 per minute. The face and conjunctivae were flushed, and there was a bright purplish generalised rash all over the face, abdomen, perineum, back, arms, legs, hands and feet. There were a few haemorrhagic and petechial spots on the abdomen, perineum, wrists, palms and soles of the feet. The rash was measly, with a few scattered papules. On the next day more papules appeared especially on the forehead, the mouth, the tongue, the soft palate, the eyelids, the external auditory meatus, the palms of the hands and the soles of the feet. The rash was never itchy at any stage. A few papules on the face, and near the hair.

line became vesicular on the 8th day of the illness and became pustular on the following day. The fever also came down by crisis and touched normal on the 10th day of the illness and remained so. The rash disappeared in about six to seven days after its appearance, with the subsidence of the fever. There were faint brownish marks left for a few days.

The patient had no headache, cloudiness of mind, or backache throughout the illness. Prostration was marked after the 3rd day but was not an initial symptom. There was some pain in the joints and muscles. Vomiting and retching, severe and persistent, were a marked feature in the early days. There was slight abdominal discomfort, but no distension or constipation. The liver and spleen were not palpable. There was no sore or ulcer anywhere on the body and there was no enlargement of the lymph nodes. The tongue was slightly coated. The lungs were clear. The pulse rate was rather slow for the fever.

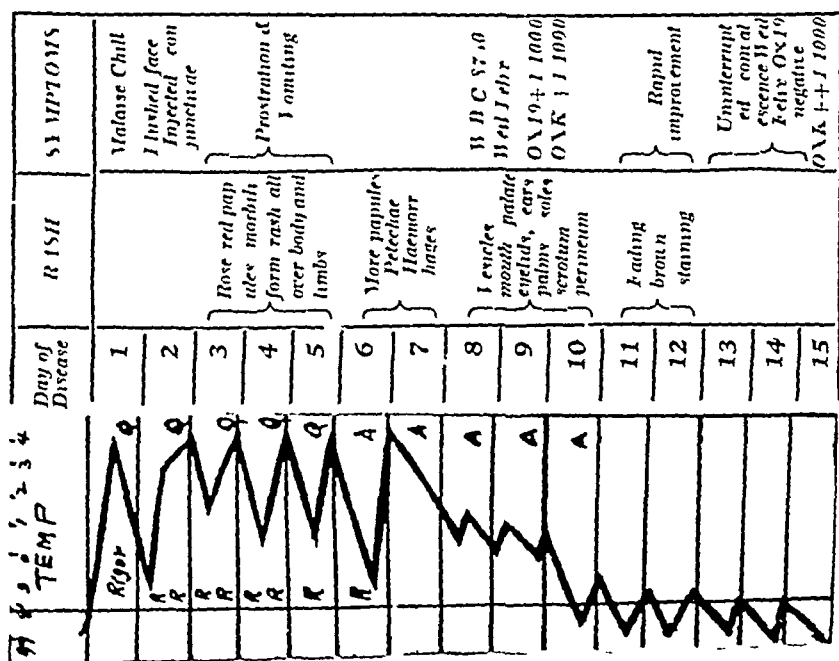


Fig 1—Showing the remittent type of fever, the evolution of the rash and the symptoms

The urine showed no abnormality except a trace of albumin. The diazo reaction was not looked for. The blood taken on the 8th day of the illness, showed 8,750 white blood cells per cmm with 56% polymorphs, 33% lymphocytes, 10% large mononuclears, and 1% eosinophils. No malarial parasites were seen. The agglutination reaction—the Widal—against B Typhosus and paratyphosus A and B, were completely negative for both O and H antigens. The agglutination reaction against the proteus group—the Weil-Felix-Wilson reaction—gave positive results for OX19 in 1 1000 dilution,

and also positive for OXK in 1 1000 dilution. This test was again repeated after 6 days, when it was negative for OX19 but positive for OXK in 1 1000.

The blood culture was negative. The Wasserman, or Kahn test and Neill-Mooser reactions and guinea pig inoculation, were not carried out.

The patient was vaccinated against small pox in infancy, though the marks of primary vaccination were not noticeable. But as a medical student and also after qualification he was revaccinated at least three times, the last vaccination being three years ago.

The patient had a similar attack of fever in December 1941, seven days after he returned from a shooting trip in the jungle. It subsided after taking quinine for two days, but he developed an itching rash, scarlatiniform and urticarial, due to quinine at that time and he is inclined to believe that the present rash was also due to quinine and the fever was probably malaria, because of the remittent character and the repeated rigors.

The patient's father had a similar fever with rash some 25 years ago when he settled in Bahrampur as a doctor, which was not diagnosed till Sir Leonard Rogers saw him and diagnosed it as tropical or tick typhus.

Was this a case of malaria with quinine rash, or a form of small pox with prodromal measly rash, or a form of unusual chicken pox or a case of tropical typhus? If typhus, was it a tick typhus or a louse typhus contracted in the train or a rat-flea typhus? If typhus, the incubation period must be very short, five days if contracted in the train, or 4 days or only 2 days if contracted in Bahrampur or in the jungle. Megaw gives the incubation period for Tick Typhus of India 5-12-20 days and for Tick Typhus of America or Rocky Mountain fever 2-12 days or longer upto 20 days.

Sporadic typhus or imported typhus is not uncommon in Bombay. I have seen cases of fever with rash which clinically suggested typhus, treated as typhoid or paratyphoid fevers, in persons who had come from the Rajpipla jungles and from Central India. One feels that in all fever cases with rash typhus must be kept in mind and serological, cultural, and animal inoculation tests should be carried out as a routine. The clinical diagnosis of typhus is difficult, and as Osler had said "it is easy to put down on paper elaborate differential distinctions which are practically useless at the bed side." The knowledge of most practitioners about the typhus group of fevers is very vague and there is a great need for detailed clinical descriptions of various types of typhus met with in different parts of India.

Analytical Review

PREVENTION OF DIABETES MELLITUS

By

C. C. MERCHANT

M.B.B.S.

BOMBAY

(Continued from the last issue p. 202)

Secondary Etiological Factors

Evidently our knowledge as regards the root cause of diabetes is quite patchy, and further study is necessary to clear it up. Whilst awaiting further information we must accept the theory of "Insulin Insufficiency"—an inheritance of the workers of the 19th century—at least for the purpose of treatment and proceed to consider those factors which are known or suspected to contribute to or provoke directly or indirectly the onset of diabetes even though in most cases, how they bring about or favour the development of the disease is not exactly known.

For descriptive purpose, the various factors may be divided into .

(I) Remote Factors—viz, Heredity

(II) Immediate Factors—subdivided into,

(1) Intrinsic factors

(a) Innate and permanent conditions—Racial and individual peculiarities e.g., sex, etc

(b) Normal variable conditions, e.g., age, weight, (obesity), exercise, and psychic influences

(c) Accidental or occasional conditions, e.g., pregnancy, past or present pathological conditions or diseases including infections

(2) Extrinsic or environmental factors, e.g., diet, occupation, climate, temperature

Extrinsic factors however important they are, cannot be separated from personal factors, as it is not the environment *per se* with which we are concerned but the patient's relation with the conditions

REMOTE FACTORS

Heredity

To day heredity is regarded as the most important factor for the development of susceptibility to diabetes though other causes such as obesity, infections, etc., are known to operate to a more or less extent. The influence of heredity has been noticed by a large number of observers (Mosley, Naunyn, Kulz, Williamson, Cammidge, and others), since Richard and Morton in 1689 first drew attention

to the probable association of heredity with diabetes. It is said that Hindu physicians knew heredity to be an important etiological factor.

However, the importance of heredity was recognized fully after the discovery of Insulin when it was made possible to study a large number of families on account of increased duration of life of the diabetics.

White and Pincus (1937) after a laborious statistical study of Joslin's large material, concluded that "the potentiality for developing diabetes is inherited and that the disease, in most cases is transmitted as a simple Mendelian recessive type," though incomplete dominant cases are not unknown. The studies of Bauer Fischer, Lenz and others also support the view of recessive type of transmission.

One of the many evidences in favour of recessive type of transmission of diabetes is the occurrence of the disease in both members of similar twins. Macklin has collected from the literature 10 pairs of identical twins in which both members developed diabetes, in five of the cases at particularly the same age. In Joslin's series of 13 pairs of similar twins, 9 pairs developed diabetes, in only two out of sixteen pairs of dissimilar twins did diabetes develop in both.

Further, it is known that the incidence of diabetes in the blood relatives of diabetics is much greater than in those of a control population—thus in a study of 4434 blood relatives of 300 diabetics, White and Pincus reported an incidence of 6.7% as compared to 1.25% in their control non-diabetic group consisting of 1290 individuals.

It is also noted that in a single family diabetes may appear at any age, but in one generation, it often appears at about the same age or period of life.

It is known that the disease has a tendency to skip one or more generations and that it is quite unusual to find evidence of diabetes in more than three successive generations. Still the disease may be introduced through marriage and may appear in an indefinite number of generations. Some writers believe that in the child of a diabetic parent, the disease runs a milder course than in cases of less direct descent. This is not always found to be true and, as a rule, the earlier the disease appears, the more severe the course it runs.

There are several views as regards the nature of the weakness or susceptibility which is transmitted.

(1) Naunyn favoured the view of inherited weakness of the sympathetic nervous system as the main cause. According to him, in sufficiently strongly predisposed subjects, the disease may develop without the occurrence of any provocation—as in the case of an

apparently normal child. In subjects less strongly predisposed, provocative factors play a part of greater or less importance according to the degree of weakness inherited.

(2) According to George Graham, it is thought that there is an inherited weakness of the Beta-cells of the Islands of Langerhans—which are known to degenerate very early in the course of the disease.

(3) The latest view and perhaps more correct, is that of Joslin who regards hereditary transmission of diabetes through the gene of the anterior pituitary body. The fact that diabetes occurs comparatively more frequently at periods of life when the anterior pituitary is known to be usually overactive, i.e., during adolescence and in women at the time of menopause, lends support to this theory.

Because the family history of diabetes is obtained only in a comparatively small number (15 to 30%) of diabetics, diabetes is often looked upon, specially by laymen as familial affection rather than hereditary. They attach much importance to the common environmental conditions particularly the dietary habits, peculiar to the family. Cases are known where the disease existed in both husband and wife, but they are perhaps examples of mere coincidence or of exposure to common family habits and environments.

II IMMEDIATE FACTORS

(1) *Intrinsic Factors*

(a) Innate and permanent conditions

(i) *Race* —In western countries, Jews are regarded as particularly susceptible to diabetes. It has been mentioned that in the city of New York, the diabetic mortality is 75% higher among Jews. On the other hand, the incidence is comparatively very small in the Japanese and Chinese. In India, diabetes mellitus is believed to be highly prevalent in Bengal, Bombay and Madras Presidencies.

On analysing 632 cases of diabetic deaths that occurred in the city of Bombay during the years 1926-36 it has been found that Parsis are the greatest sufferers from diabetes. Looking to their comparatively very small population, 50,000 in all told, the number of deaths—181 among them should be considered as a serious matter requiring careful and urgent investigations with the view of an early and effective control of the disease among them.

The following TABLE shows the number of deaths amongst the different communities of Bombay City, out of the total of 632 during 1926-36

Community	No. of deaths
Hindus of all classes	249
Mohamedans	122
Parsis	181
Jews	3
Indian Christians	60
Europeans and Anglo Indians	17

(ii) *Sex* —According to Joslin, in childhood and early adult life mostly upto the age of 35 years, there is very little difference in the incidence and death rate between the two sexes but after this age, the death rate in females (58.2%) shows a slight preponderance over that in males. However, in India, obviously more males are known to be treated than females. The proportion between deaths among males and females studied by Dr Bose is found to be 3 : 1 (1159 males to 341 females). However, on taking the figures for Indians and Europeans separately and then comparing the figures for male and female deaths a marked difference is found in the proportions. For Europeans, the proportion is found to be 1 male to 1.2 female, whilst amongst Indian the ratio between male and female deaths is found to be 5 : 1.

The proportion between male and female deaths among the total of 632 deaths previously mentioned is found to be 2 : 1 (421 males and 211 females). But when different communities are considered proportions are found to vary greatly between male and female deaths, as seen from the following TABLE

Community	No. of deaths	
	Male	female
Hindus including Jains, Brahmins & Bhatias	180	69
Mahomedans	75	34
Parsis	96	85
Jews	1	2
Indian Christians	36	24
Europeans & Anglo Indians	10	7
Total	411	221

Dr Bose (1937) thinks that the low incidence of disease among Indian women, specially the Hindus and Mahomedans is in all probability an apparent one, and does not show the real state of affairs. The peculiar social and religious customs coupled with illiteracy and their peculiar shyness, are hindrances to their seeking medical help, unless they are seriously ill or suffer from a severe painful condition, and thus many cases are not brought to light. Further high incidence among Parsi women may be due to the fact that the community is far advanced in civilization and the Parsi women are exposed more or less to the same adverse environmental conditions as their men folk.

(b) Normal Variable Conditions

(i) *Age* —No age seems to be exempt and diabetes may occur at any age from birth to 90 years. However, the majority of cases occur during the middle period of life i.e., between 40 to 60 years. According to Joslin, the susceptibility to the development of diabetes becomes marked between 30 to 35 years and rises to its maximum between the years 51 and 55, and thereafter it declines. Persons developing the disease after the age of 60, usually suffer from a mild form of diabetes. It is rather difficult to ascertain the exact time

of onset of the disease in the older persons, on account of the slow and insidious onset of the disease in them. The peculiar susceptibility to develop diabetes in the middle period of life has been explained as being due to changes in the endocrine glands which are more marked between the ages of 40 to 50 years (in women at the menopause period). The older the diabetic grows, the greater is the chance of his dying from diabetes, this is assumed because the mortality rate increases with age and reaches its maximum at an age period between 60 to 70 years.

Diabetes in children is not at all rare, and in them the onset is usually acute. Two deaths in infants under 7 days and three deaths in children between 1 and 5 years have been recorded among the 632 deaths for the Bombay city (1929-36), as shown in this TABLE.

Age period	No of deaths
Under 7 days	2
" 1 year	1
Between 2 to 5 years	2
" 5 " 15 "	"
" 15 " 20 "	11
" 20 " 30 "	28
" 30 " 40 "	51
" 40 " 50 "	136
" 50 " 60 "	182
60 years and over	216
Total	632

It is believed that on account of the peculiar climatic conditions and almost exclusive vegetarian diet taken by a larger proportion of its population, the onset of diabetes occurs earlier in Indian than in the Western countries.

(ii) *Obesity* —Associated probably with heredity and endocrine dysfunction, obesity is considered to be an important predisposing factor, for the simple reason that diabetes occurs more frequently in obese than among persons of normal weight and size. Joslin refers to "diabetes" as the man's folly, and "obesity" as the open door to diabetes. Dr. Bose of Calcutta obtained a definite history of previous obesity in nearly 50% of the cases that came under his observation.

Allen (1920) observed in dogs experimentally made diabetic by partially extirpating the pancreas that the Insulin requirement was much less in lean than in fat dogs. These experiments are important in showing the relationship between obesity and the severity of the diabetic condition.

What exact role obesity plays in the development of diabetes has not yet been definitely demonstrated. It is commonly suggested that both obesity and diabetes owe their origin to excessive ingestion of carbohydrate combined with lack of sufficient exercise (Lambie 1935). The increase in weight which occurs after Insulin treatment in non-diabetic persons often resulting in actual obesity gave a hint that

obesity might primarily be due to hyperactivity of the Insulin producing cells stimulating formation of fat and he (1928) ascribed certain cases of obesity to insulogenic causes. He found that in cases where rapid increase of weight took place there was always increased secretion of Insulin.

The development of diabetes in such cases of obesity has been explained as follows—It has been found that in obesity whether due to overeating or due to endocrine disturbances two well marked changes usually occur, viz, (a) excessive conversion of carbohydrate into fat together with diminished combustion of fat by the tissues, —as manifested by the diminished respiratory quotient (Bagedorn and co-worker 1927, Lyon 1932, Gardiner and Hill), and (b) gradual decrease in sugar tolerance with the duration of obesity (Nissler, Gordon and co-workers, Von Stanley 1930, Ogilvie 1935).

As a result of comparatively greater demand made on carbohydrate due to lessening of fat combustion coupled with excessive conversion of carbohydrate into fat, the amount of carbohydrate actually available for combustion in the tissues is much less than that actually needed for energy purposes. As a result, an obese person suffers from usual symptoms of hypoglycaemia such as weakness, nervousness, fatigue, nausea, giddiness, craving for sugar and sweets, etc. As a result he increases his food intake but lessens his exercise—both the acts greatly favouring further development of obesity. Moreover hypoglycaemia has been found in a larger number of early cases of obesity whilst in the older cases, hyperglycaemia is generally observed. In intermediate cases the blood sugar is usually found to be maintained at normal levels. These observations have been explained as being the result of gradual exhaustion of previously hyperactive Islet cells of Langerhans.

Dr Bose (1937) found diminished sugar tolerance in varying degree in nearly 40% of persons who came under his observation and who were quite normal except for their weight in relation to their height and age.

Obesity with a decrease in sugar tolerance should be looked upon as a dangerous forerunner of diabetes mellitus (Duncan 1933) and should be early recognized and treated from the very start by cutting down the excessive intake of carbohydrate—the latter being a common etiological factor in the development of both obesity and diabetes (Nissler and Gordon).

Another view regarding the association of diabetes with obesity is that both the disorders primarily arise as a result of dysfunction of the endocrine glands specially the anterior pituitary.

On the other hand Nissler suggests that most of the cases of obesity are really due to overeating and that endocrine disturbances are perhaps the result of obesity rather than its causes.

It has been mentioned that in obesity there is a great deal of fatty infiltration in the pancreas including the Island tissues which

greatly reduces the normal secretion of Insulin by the Island cells
The validity of this statement is not yet proved

Obesity is associated with hypercholesteremoelia which it is said, may lead to gall stones and subsequent infection of the gall bladder. The infection may spread through the common bile duct into the pancreatic duct and may cause sub-acute pancreatitis and later diabetes. If at all diabetes is produced in this fashion, it must be only in a very negligible percent of cases.

By accepting obesity as a forerunner of diabetes, it would be easy to conceive that any condition which favours the development of obesity will also directly or indirectly help to induce diabetes. Therefore, increased income in the family, which would permit greater indulgence in rich diet, increased leisure due to increased use of labour-saving devices, and sedentary occupation may contribute to a varying extent to the development of diabetes.

(iii) *Sedentary habits and lack of exercise* —Both have long been recognized as important factors in the causation of diabetes, especially in persons who are prone to it. Diabetes is seen as a rule, more frequently among persons of sedentary habits and occupation than among those who do a certain amount of manual work. The rapid increase in the incidence of diabetes during recent years is considered to be due to the rapidly changing conditions of modern life in which machinery and electric power have greatly replaced human labour. In modern industry everything is done to minimise human labour and to increase production, at the cost of more brain work (skilled labour). The influence of exercise is reflected in the greater incidence of diabetes in cities than in villages, because of easier work, and more leisure inherent in the city households and greater transportation facilities.

Exercise is known to cause more of the muscle sugar to be burnt as is shown by a rise in the respiratory quotient (Hill), and to improve glucose tolerance (Allen) as is shown by a lowering in blood sugar level and a decreased amount of sugar in the urine. Exercise in a diabetic person is known to diminish his Insulin requirement in order to keep the urine sugar free.

Dr. Bose (1937) experimenting on a diabetic patient with a view to find out the effect of exercise found the following changes in blood sugar concentrations after Insulin injection with and without exercise. The figures clearly show increased sensitivity to Insulin as a result of exercise.

Time	without exercise	with exercise
	Blood sugar	Blood sugar
At the start	0.208%	12 units of Insulin
8 A.M.	0.168%	0.132%
9 A.M.	0.123%	0.084%
10 A.M.	0.125%	0.035%
11 A.M.		

On the day after exercise, the patient complained of symptoms of mild hypoglycaemia

Exercise by causing an increase in the size of the muscles greatly increases the capacity to hold glycogen, and this may have a beneficial effect in the utilization of carbohydrate

(iv) *Psychical and nervous conditions*—It is stated that nervous disturbances play an important part in the life history of a large majority of the diabetic patients

Psychical shocks or frequently occurring powerful emotions, fatigue both physical and mental, worries, anxieties and moral sufferings arising from domestic infelicities, financial losses and failure at examinations or important elections are considered to be important contributing factors in the development of diabetes or at least in precipitating its onset

Present day uncertain economic conditions and rapid changes in social adjustment are world wide matters and general anxiety practically affects all classes of people rich or poor, young or old, men or women, though intellectual ones are particularly more liable to be affected and pay a heavier penalty than the rest

Constant anxiety sooner or later may produce hypertensive but rather unstable state of the nervous system, both cerebrospinal and autonomic—resulting in a variety of somatic as well as psychical disorders such as dyspepsia, constipation, anorexia, insomnia, etc

With a terrain thus prepared, especially in persons prone to diabetes either by reason of heredity or obesity, any additional worry, anxiety, or sorrow or disappointment, arising from causes like illness of a near relative, acute monetary difficulties, insecurity of service, unexpected failure in one's undertakings, may act as a powerful stimulus to the onset of the disease. In fact, many diseases besides diabetes are, to-day considered to arise primarily from the disturbed states of the nervous system. They are hyperthyroidism, bronchial asthma, peptic ulcer, and Raynaud's disease

The fact that diabetes occurs more frequently (a) in cities rather than villages (b) in highly civilized communities and (c) in young to middle aged persons who are rather dynamic in outlook than lethargic, lends support to the neurogenic origin of diabetes. Further evidence is supplied by the now known existence of vegetative centres in the brain as well as by the fact that the liberation of Insulin in the blood especially that required for the rapidly changing needs of the body is controlled to a certain measure by nerve impulses through the vagus

Further it has come within the observation of many clinicians that in a large number of cases the onset of diabetes is preceded by a severe nervous shock such as may result from injuries from an automobile accident, fall from a height, heavy blow on the head or abdomen, or a severe and protracted operation

Joslin, Von Noorden, Umber, Labec, on the other hand do not regard trauma or the mental or emotional shock following an injury, to be either a direct or indirect cause of diabetes. Joslin considers that if trauma were much of a factor in the causation of diabetes the world war would have shown it. He regards that statistical evidence is rather in favour of a decreased incidence among both the army and civil population rather than in favour of an increase. But he recognizes the adverse effects of trauma in diabetes in so far that (1) it may activate the latent or dormant disease and cause to break forth perhaps at an earlier age in an individual predisposed by heredity to become diabetic at a given age or (2) it may make the actual disease more severe.

In any case, trauma or injury is inimical to diabetes as it tends to shorten the life of a diabetic and should be avoided as far as possible.

Various injuries and diseases of the central nervous system such as concussions, skull injuries, apoplexy, brain tumours, specially of the pituitary and the mid-brain are known to be attended with glycosuria which may or may not be diabetic.

(c) *Accidental or Occasional Conditions*

(i) *Pregnancy* —It has a marked influence upon carbohydrate tolerance as well as the diabetic condition. Very often temporary glycosuria is found in women during the pregnant state, at times glycosuria persists and is usually diabetic in nature. In an existing diabetes, pregnancy usually aggravates the condition at first, but during the later part or after its termination the symptoms become milder or may disappear. Pregnancy diabetes is perhaps due to the changed relation between the oestrogenic principles and the anterior pituitary glands. Statistical figures collected by Joslin do not point to pregnancy as an inciting cause of diabetes. If pregnancy was a cause, then diabetes should have been found more in females under 45 years than in males of the same age. But this is not the case. Diabetic incidence in females is usually high when the pituitary prolapse is high and at such times when existing diabetes is made more severe as at ages between 11 and 13, and 45 to 55 years. Diabetes is more difficult to control during catamenia and at the time of menopause.

(ii) *Infections* —It is very doubtful whether diabetes is due to any specific micro-organism. Bergey D H (1926) suggested that diabetes was produced by a transmissible infective virus which passed through the Berkfield filter. He produced in rabbits an intermittent glycosuria by the intravenous injection of 2 cc of diabetic urine after being passed through a Berkfield filter. He also found that the urine of the rabbit made so diabetic produced diabetes when injected into other animals. His work has not however been corroborated by other workers.

The same holds true for the plasmodium of Rasch (1920) (Macfarland—Proc Path Society 1920, 23 p 92) Though no known micro-organism can yet be said to directly cause diabetes still it is a matter of common knowledge that diabetes very frequently breaks forth after an infection, which may be as mild as a common cold, and that in existing diabetes, symptoms usually become worse during illness, and that the Insulin requirement is substantially increased in order to keep the urine sugar free

In actual practice most of the cases of diabetes are brought to light either during or soon after an acute illness such as tonsillitis, typhoid fever, parotitis, perhaps through routine urine examination

It is not uncommon to come across patients whose urine was sugar free before the appearance of carbuncle, developing glycosuria during the active stage, and requiring 50 or more units of Insulin per day to keep the urine free from sugar Very often with the improvement in the clinical condition, glycosuria lessens or even disappears, on the other hand, the diabetic condition may become worse and too difficult to control

How infection affects sugar metabolism is not at all known The probabilities would seem to be (1) a decreased supply of endogenous Insulin, (2) destruction of Insulin after its production, (3) an upset in the capacity of liver to store glycogen, (4) the production of some hormone antagonistic to Insulin

Lawrence and Buckley showed experimentally that diphtheria toxin almost totally inhibited the action of Insulin There is also a certain amount of experimental evidence to show that Insulin content of the pancreas is decreased in certain infections, though it is not known whether the liberation of Insulin is actually interfered with

It has been suggested that products of disintegration of pus cells which are found to inactivate Insulin in vitro, destroys Insulin in the body, but this has not been proved experimentally in vivo

It has been found that during any infection, liver glycogen is much diminished Hence it is thought that the suprarenal and thyroid glands are stimulated as the first effects of the products of infection in order to release more of their internal secretions The secretions in turn either cause increased break down of liver glycogen with resulting hyper-glycaemia or interfere with the synthesis of glycogen from lactic acid in the liver In both cases, the Insulin insufficiency is relative

Recently, Wien produced pyrexia in animals by injecting a killed culture of *B. Coli Communis* and did not observe a rise of blood sugar, but on injecting in these animals 0.5 unit of Insulin per kilo body weight he found no fall in blood sugar level When the same experiments were repeated in hypophysectomized rats and in adrenalectomized or thyroidectomized rats and cats,

he found that there was very little effect on the normal Insulin sensitivity, though pyrexia was somewhat lessened in intensity. He has suggested, therefore, that in bacterial infections, the pituitary, thyroid and adrenal may be all concerned in the production of bacterial pyrexia as well as in the development of resistance to the hypoglycaemic action of Insulin (Lancet P 505, 26-2-38)

Very often diabetes is known to follow recovery from an infectious disease specially the typhoid. Joslin regards the development of diabetes in such cases as being due to the rapid development of obesity rather than due to the infection per se. Convalescents usually have big appetites and are usually overfed with a great zeal, especially during the period of comparative inactivity and when the pancreas requires to be rested.

(iii) Disease of other organs —

(1) *Affections of liver and gall bladder* — Since the time of Claude Bernard who first studied the glycogenic functions of the liver, it has been looked upon as one of the principal organs involved in the production of diabetes. Diseases of the liver, e.g., acute or chronic hepatitis, cirrhosis, new growth have often been found to be attended with glycosuria, how far the latter is diabetic in origin, it is difficult to say. Dr Bose (1937) is of opinion that glycosuria seen in infantile cirrhosis of the liver is not diabetic in nature. On the other hand, affections of the gall bladder (cholecystitis and cholelithiasis) which are common findings in the middle aged obese persons have often been found to be precursors of true diabetes. Infected bile has been shown to be capable of causing pancreatitis and many diabetics are known to have suffered from recurring attacks of sub-acute pancreatitis.

(2) *Mumps* — On account of close similarity between the pancreas and parotid in their microscopical structures and the fact that mumps has occasionally been followed by an acute attack of pancreatitis, mumps has often been blamed as a cause, for at least some cases of diabetes.

(3) *Arterio-sclerosis* — It is very doubtful whether arterio-sclerosis is the cause or the result of diabetes. In any case, its presence in a diabetic should be seriously looked upon as it is a cause for many complications such as gangrene of the extremities, retinitis, resulting in blindness, and weakened circulation—which are all very difficult to control.

If arterio-sclerosis be accepted as a cause of diabetes, it may be supposed to act by interfering with the blood supply of the pancreas and liberation of Insulin by the Island cells. Arterio-sclerosis is now-a-days considered to be a complication of diabetes rather than its cause, developing at a time when diabetes is most likely to manifest itself. The relationship between the severity of the arterio-

sclerotic lesions and the severity of the diabetes is not constantly observed. Very frequently it is found that arterio-sclerotic changes are most marked but still the diabetic symptoms are comparatively very mild, on the other hand arterio-sclerotic changes are found to be absent or most insignificant in cases suffering from severest form of diabetes especially in young subjects.

(4) *Syphilis* —This disease has often been attributed as a cause of diabetes, but intensive anti-syphilitic treatment has not proved to be of any value except in rare cases.

(5) *Asphyxia and poisons* —Anaesthetics like chloroform and ether, coal gas and carbon monoxide usually cause glycosuria, probably by producing asphyxia. The latter causes excessive secretion of adrenaline and accumulation of acid products of metabolism. Both these factors are known to interfere with action of Insulin and produce glycosuria.

(2) *Extrinsic or Environmental Factors*

(1) *Diet* —“Tell me what you eat. I will tell you what you are.”—*Brillat Savarin*

Every physician knows that diet plays an important part in the causation of diabetes and that the disease is seen particularly in private practice, chiefly amongst the well-to-do class of people who are generally over-weight for their age and height. Still, it is not yet established what part diet plays in precipitating the onset of diabetes. It is not yet ascertained whether the fault lies in quantity or quality of the diet. The main difficulty in elucidating the problem of diet in diabetes lies in the fact that the methods of the laboratory—possible in the case of experimental animals—are not applicable to human beings. The diet of an experimental animal can be chosen with meticulous care as regards quantity as well as quality but in the case of man the choice of the diet is greatly determined by a number of factors, viz, racial and family customs, individual taste, appetite as well as food materials available and the economic condition of the subject.

Lack of exercise and indulgence in the pleasures of table are generally advanced as causes mainly responsible for the onset of diabetes. However it is not uncommon to find gluttons who develop neither obesity nor diabetes, on the other hand, cases of diabetes are not rare amongst the poor classes—even the beggars, but then the disease is severe and found in young subjects.

There is experimental evidence to show that overfeeding alone is not sufficient to produce diabetes, but that it is greatly influenced in its results by certain other conditions. It is possible that diet which is sufficient to prevent clinical signs of diabetes under one set of conditions may actually cause the disease to become active under quite a different set of conditions.

Such a diet possesses less stimulating effect on metabolism on account of lessened protein intake and consequently the general metabolism of the body is much lowered. In this way obesity and diabetes may be brought about by a diet relatively deficient in protein, but otherwise normal. Excess of fat with relative deficiency in protein and carbohydrate (anti-ketogenic factors) is said to bring about sclerotic changes in blood vessels, including those of the pancreas—interfering with the proper supply of blood to the Insulin producing Island cells.

Lack of vitamins in diet—Several investigators Peter and Thompson (1934) Tiszwitz (1937), Azode and Masone (1937), Gringoire and Mills have shown the beneficial effects of vitamin B1 complex on carbohydrate metabolism particularly in diabetes. The failures with this treatment according to Vorhuns, Williams and Waterman are due to inadequate doses (Bayer Records June, Sept, Octr 1937, Merk's Betablon).

Peters, H M Sinclair and Thompson (Lancet Vol I, p 1161-1936), found during their studies on vitro respiration with the brains of pigeons that with vitamin B1 deficiency there was a specific accumulation of pyruvic acid, whereas in the presence of this vitamin pyruvic acid did not accumulate. This experiment implicates that pyruvic acid a normal intermediary product in carbohydrate oxidation cannot be further oxidized in the absence of vitamin B1. Thompson and R E Johnson, since then, found in animals suffering from Vitamin B1 deficiency, pyruvic acid abnormally collected in the blood, disappearing when the deficiency was cured.

The abnormally high glucose tolerance curves observed by Lepkovsky in rats showing signs of B1 deficiency is another evidence of a disturbance of carbohydrate metabolism.

These observations suggest that B1 plays the role of a co-enzyme in the oxidative enzyme mechanism of the tissues concerned in the intermediary metabolism of carbohydrates.

Hence a diet which is deficient in Vitamin B1 complex may strongly favour the development of diabetes. Refinement of our foodstuff greatly deprives us of those parts of the cereals (germ and inner layers of bran) which contain the essential Vitamin B1 and may reasonably be considered as a potent factor in the causation of diabetes. With mixed food and daily quantity of milk we obtain sufficient Vitamins A and D. But, on the other hand, in diet chiefly composed of carbohydrates in the form of white bread, rice, etc., usually B vitamin may be lacking to a varying degree. Vegetables it is true, contain Vitamin B1 but not great enough to make up for the deficiency in the cereals.

Rollew (1936) found that Vitamin A lowered sugar tolerance and caused glycosuria whilst Vitamin C produced an opposite kind of effect.

(ii) *Occupation and profession* —“Incidence varies with chances of becoming overweight”

Statistical evidence points out the fact that diabetes is much more prevalent amongst persons engaged in professional callings such as lawyers, doctors, and teachers, and in clerical and mercantile pursuits such as industrial magnets, bankers, clerks and big land holders who do mostly mental but very little physical work than in persons whose occupation requires more labour than mental work. In general terms it may be said that whenever conditions of life are easy with plenty of leisure and plenty to eat, both obesity and diabetes are prone to develop

The TABLE given below shows the diabetic mortality per cent according to occupation amongst 1,500 cases collected by Dr Bose (1934)

Land holders	22 3%	Physicians	9 1%	Engineers	3 7%
Merchants	16 8%	Teachers	6 5%	Police	1 9%
Lawyers	15 2%	Clerks	6 3%	Ry Officers	7%
		Unclassified	4 2%		

It is considered that strenuous mental work combined with anxieties or worries plays an important role in bringing on the actual attack of diabetes specially in persons who are predisposed or suffer from latent diabetes. The dictum “Mental work makes sugar and manual work breaks it up,” is worth remembering

(iii) *Climate* —It has been mentioned that diabetes is comparatively more common in tropical and sub-tropical countries and this opinion seems to have been based mainly on two observations viz, (1) that the principal food in tropics is rice or any other form of starch and (2) that a large number of Europeans returning home after a long stay in tropics have been found to suffer from diabetes. It has been stated that in tropical and sub-tropical climates, there is a tendency for lowering of carbohydrate tolerance and according to Basal Smith (BMJ 31 July, 1926), for retaining CO_2 in the alveolar air when the subject is at rest

Observations made by Dr D Zel Zion of Palestine (1932) are interesting and they are (1) that the sub-tropical climates of Palestine and hot tropical regions in particular, cause a lowering of carbohydrate tolerance in the newly emigrant persons, and in many cases glycosuria results, (2) that a considerable improvement in the condition occurs after leaving Palestine, (3) that the diabetes is comparatively severe in the hot regions of Palestine than in cooler mountainous regions, and (4) that the course of the disease is more severe in summer than in winter

of their cases, and in these, the symptoms were those of tetany and not those characteristic of the Effort syndrome. This experiment affords good evidence against the theory of hyperventilation in relation to the Effort syndrome.

R J VAKIL

PULMONARY ENDARTERITIS IN CASES OF RHEUMATIC HEART DISEASE

Bredt, H and Stadler, L Arch F Kreislaufforsch, 7 54 (1940)
abstr Amer Heart Jour 21 535 (1941)

Bredt and Stadler have made a microscopic study of the pulmonary vessels in 37 cases of rheumatic heart disease with valvular involvement. Certain reactions of an inflammatory nature e.g. proliferation of the intima, narrowing of the lumina and changes in the media were described in the arteries, veins and smaller vessels. Certain symptoms in the clinical picture of these heart cases viz dyspnoea and cyanosis were regarded as possibly secondary to these inflammatory changes in the pulmonary vessels (Pulmonary Endarteritis).

R J VAKIL

SULFONAMIDES IN THE TREATMENT OF ERYSIPELAS

Robert F Shank, M D, Richard W Maxwell, M D, and George S Bozalis, M D, (J A M A, Vol 117, Dec 27, 1941) p 2238

The authors' conclusions are —

(1) One hundred and sixty-five consecutive erysipelas patients in the St Louis Isolation Hospital were treated with sulfonamides, with a mortality rate of 3 per cent. Patients over 60 years of age, with chronic heart and kidney disease, furnished 4 of the 5 fatalities among this group.

(2) In no instance was the lesion even seen to spread after the first thirty-six hours on chemotherapy. A small sub-cutaneous abscess was the only complication. There were no recurrences.

(3) In 84 patients an elevated admission temperature had returned to normal after twenty-four hours and remained normal. In 16 cases fever persisted over forty-eight hours but in no instance longer than four days.

(4) Sulfanilamide was found to be fairly toxic, particularly for the aged patients in this series. The new drug sulfabenzamide, used experimentally for 34 patients, produced equally good results, without the usual toxic effects so common to the sulfonamide group of drugs.

(5) The prompt response of erysipelas to the sulfonamides makes this the treatment of choice and renders other therapeutic measures obsolete.

THE USE OF SULFACETIMIDE (ALBUCID) IN BACILLARY INFECTIONS OF THE URINARY TRACT

Welebr and Barnes, (JAMA Dec 20, 1941, pg 2132), have used albucid (Schering) in 200 cases of bacillary infections of the urinary tract. Albucid or sulfacetimide is a sulfanilamide derivative (p amino-benzene-sulfonyl-acetyl-amide). Albucid has weakly acid properties and it readily forms easily soluble salts in the alkalis and is rapidly absorbed from the gastrointestinal tract. It was found that the average blood concentration during the course of administration (4.5 Gm a day) was 3.1 mg per hundred cubic centimeters and there was complete elimination six days after the last dose had been taken. It was found that the blood concentration reached a maximum of 7.9 to 8.1 mg per hundred cubic centimeters two hours after the oral administration of a single dose of 4 Gm of the compound. It is eliminated in a large part unchanged, by way of the kidneys. Kidney function has a bearing on the elimination curve. After discontinuance of the drug there is a steep drop in the elimination curve and by the sixth day after the last dose has been taken the body is practically free of the drug.

This report covers a series of 200 cases. Each case presented gram-negative bacilli demonstrated in the urine either by stain or by culture. No value was placed in the pH of the urine, as it was found that the albucid was as effective in acid as in alkaline urines. The course of treatment lasted 10 days, consisting of 34 tablets given in the following manner: two tablets after meals three times a day for three days, and then one tablet after meals three times a day for two days and ending the course with one tablet twice a day for five days. A course of 15 Gm (30 tablets) was as effective in the large majority of cases. The patients with bladder complications required larger doses. About four per cent of the cases had side reactions such as nausea, vomiting, dizziness, palpitation, tachycardia, precordial pain, cyanosis, maculopapular, itching rash or erythematous rash. After discontinuance of the drug, the reaction disappeared within a period of 1 to 6 days. Of the 200 cases of bacillary urinary tract infection treated with albucid, 85.5 per cent recovered, 12.5 per cent showed improvement and 2 per cent showed no response to the drug. The average number of days for recovery was 10 days, the maximum 34 days and the minimum 4 days. In the authors' opinion, albucid has been more effective in the treatment of these infections of the urinary tract than sulfanilamide and mandelates. In 80.9 per cent of the sulfanilamide-resistant cases, in 73.3 per cent of the mandelate-resistant cases and in all of the sulfathiazole-resistant cases recovery occurred when sulfacetimide (albucid) was given.

CHANCROID**TREATMENT WITH SULFATHIAZOLE AND SULFANILAMIDE**

*Borris A Kornblith M D, Adolph Jacobs M D and Louis Chargin, M D,
(J A M A No 117, No 25, Dec. 20 1941, P 2150)*

(1) A series of 175 consecutive ambulatory patients with chancroid infection were treated with sulfanilamide and sulfathiazole

(2) The identification of the Ducrey bacillus on smears stained by the Unna-Pappenheim method (methyl green pyronine) was found to be the most important single diagnostic criterion of chancroidal infection

(3) The intradermal reaction to Ducrey vaccine proved to be specific and was found positive in about 95 per cent of cases

(5) The Ducrey vaccine test is more important when the results were negative, to exclude active chancroidal disease. When the reaction is positive it often indicates a past, healed infection

(6) The reaction to Ducrey vaccine remained positive in all cases after complete healing of the active lesion had taken place

(7) Chancroidal buboes were present in about 42 per cent of the cases

(8) Sulfanilamide was administered orally to 150 patients for fourteen days, a total of 45.6 Gm in divided doses was found adequate

(9) Sulfathiazole was administered orally to 25 patients for ten days, a total of 20 Gm in divided doses sufficed

(10) All definitely proved chancroidal infections healed with chemotherapy

(11) Surgical measures of any description were contra-indicated and found unnecessary

(12) Aspiration of large inguinal abscesses was found sufficient in some cases. Spontaneous absorption of small abscesses took place in 5 cases during chemotherapy

(13) Reinfections occurred in 5 cases, and there was 1 questionable relapse, all the lesions healed promptly with a second course of chemotherapy

(14) Local application of sulfathiazole powder healed superficial chancroidal ulcerations. In 2 patients a relapse occurred, but the lesion responded promptly to oral therapy with sulfathiazole

(15) More than half (54 per cent) of the patients in our series were found to be infected with two, three or four venereal diseases during their observation

(16) Sulfonamide therapy may be used as a therapeutic test in the differential diagnosis of chancroid

AUTHORS' CONCLUSIONS

SULFATHIAZOLE IN GONORRHEAL URETHRITIS

William Broome, (J A.M.A. Dec , 20, 1941, pg 2135) has used sulfathiazole in preference to sulfonamide in 100 patients suffering from Gonorrheal Urethritis. The age varied from 22 to 46. All men were employed in heavy industries and actively working. 40 per cent of the series had experienced one or more previous attacks of gonococcic infection. The evidence of urethral irritation appeared uniformly four days after exposure. 36 per cent of the group had received treatment with sulfanilamide before they became part of this series. The dose of this drug had ranged from 1 to 3 Gm daily and had continued from 7 to 49 days without alteration of the clinical evidence of the disease. The total dose of sulfanilamide involved ranged from 9 to 49 Gm. In all cases urethral discharge revealed gram-negative intracellular diplococci and all were cases of acute gonococcic urethritis. The dosage of sulfathiazole was as follows. The total initial daily dose varied between 3 and 7 Gm, the average approximating 4 Gm. This daily dose of 4 Gm was divided in four parts and given at approximately equal intervals during the hours of the patients' activity. This dosage was maintained from two to eight days, the average being somewhat less than five days until cure was attained. The average total dose for this period was 18.4 Gm.

Forty per cent of the series required no further sulfathiazole because smears had become negative within this period and had remained negative for a period of thirty days of observation following the first negative smear. On the average, negative smears were obtained within three days on 4 Gm daily. Sixty per cent of the series required further doses of sulfathiazole for cure, and the average additional amount of the drug was 8.2 Gm, which represents slightly more than 2 days of additional medication.

The diagnosis of cure was based on (1) inability of finding a urethral discharge for staining purposes and (2) persistently negative culture of the urine for traditionally provocative tests. In all cases the ingestion of alcohol was utilized as a provocative measure and, in quite a number, protected coitus.

The period of actual therapy and close observation included a period of three to thirteen days, and in this time 100 per cent of the series was cured. All were observed for an additional thirty day period. No local medication was utilized in this series, and there were no local complications of the disease and no reason to anticipate the development of stricture in the future.

Of the toxic reactions, 23 per cent of the patients complained of nausea, but there was no vomiting. 5 per cent manifested elevation of temperature. In one patient a diffuse, discrete, pruritic, papular eruption developed which was demonstrated to be scabies. There were no instances of haematuria, oliguria, or anuria. Following the works

of Curtis, the entire series had the concurrent administration of a urinary alkalizer (a citrate) orally, and were urged to force fluids to capacity. No patient lost time for work. This series has convinced the author that there is no need for the continued use of other routines of treatment in conjunction with sulfathiazole. No local treatment is at all necessary. The author feels that the dosage must be high from the start, there is no justification for a dosage schedule which tends to start at a low level and then builds up to what is known to be an adequate dose. This method is likely to produce drug resistant types of bacteria. The author does not advocate repeated determinations of the amount of the drug in the blood to evaluate progress of therapy. The observation of clinical progress was quite dependable and the information to be gained from the study of the urethral discharge and the urine was quite sufficient, and the routine determinations of the blood level was a thoroughly unnecessary additional expense to the patients. The author's conclusions are

(1) Sulfathiazole is capable of curing gonococcic urethritis in the male quickly when administered orally in doses of 4 Gm daily. This dosage should be continued for a time after there is clinical and bacteriologic evidence of cure.

(2) On this dosage, the appearance of complications due to drug toxicity are rare and should not impel one to shun the drug.

(3) The estimation of the blood level in the face of easily obtained clinical evidence is an unnecessary procedure.

(4) Traditional adjuvant routines of therapy are not necessary.

(The strain of gonococcus encountered by Bromme appears to be of low virulence.)

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The Indian Physician

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Let us remember

CHARLES NICOLLE

By

R S (*Hans Zinsser*)

How fervently I have often wished that my parents had been pious Christians and that, in the plastic years of childhood, before I had learned to think, my mind had been moulded in the comfortable belief in a life after death! How pleasant it must be to look placidly forward to rejoining in heavenly surroundings of one's own imaginative preference, those who have made our lives on earth richer and happier. The thought of death would be considerably mitigated for me by the expectation of seeing again — among others — Charles Nicolle, and renewing for a piece of eternity those summer evenings at Sidi-bu-Said where, as the cooling breeze came up from the sea, we walked together chatting of relapsing fever, trachoma, dysentery, brucellosis, Carthaginian archaeology, Roman mosaics, mediaeval legends, French Encyclopaedists, and many other things dear to our hearts. And heaven might do worse than appear like Sidi-bu-Said, with the evening sun golden on the quiet waters of the Gulf of Bizerta and cloudless sky darkening over the high shore where Carthage once stood. And if, together, we could have a small celestial laboratory and discover a few avian diseases like psittacosis, roup, or fowl-pox among the angels, paradise were paradise indeed. Except for the infected angels, we had all these things, more or less, in Tunis for a little while.

I went to Tunis entirely on Nicolle's account. For years we had been in correspondence. In 1915, we had a rendezvous

for work together in the Balkans, but the French Government needed him at that time and our meeting was postponed. Already even then, he was beginning to stand out as one of the great living bacteriologists—with no contemporary peers, in my judgment, except Bordet, Landsteiner, and Theobald Smith. The World War and the intervening period of concentration on theoretical problems had, for ten years, carried me away from the fields of work in which he had gained distinction. But in 1928, again returning to problems of typhus fever, I wanted to see him. Differences of opinion had arisen, new methods had been devised, and correspondence was unsatisfactory.

It was the beginning of a friendship that started in our heads and soon extended to our hearts. North Africa is an El Dorado for the student of infectious diseases. There are Malta fever, *fièvre boutonneuse*, relapsing fever, typhus, kala-azar, leprosy, malaria, and odds and ends of tropical infection that come up from the oases in the south. There were many things to learn and much to discuss, and I was especially interested in trying to overcome some experimental difficulties by transmitting typhus to monkeys with human lice. Nicolle received me with open arms. He gave me a laboratory, a technician, and all the materials I needed—even to a supply of bearded Arabs, who furnished the insects. Best of all, he gave me his friendship.

Nicolle was one of those men who achieve their successes by long preliminary thought, before an experiment is formulated, rather than by the frantic and often ill-conceived experimental activities that keep lesser men in ant-like agitation.

Indeed, I have often thought of ants in observing the quantity output of "what-of-it" literature from many laboratories. I once watched a swarm of ants, on a lazy summer afternoon, and wondered why they had acquired the reputation for sagacity attributed to them by sentimental entomologists. One ant, I observed, was carrying a weighty bit of straw from one place to another, obviously making heavy weather of it. Instead of going around grass-blades and sticks, he laboriously climbed over the tops of them, then painfully fell off and trudged onward—passing on the way, and even finding at his destination, bits of straw quite equal in beauty, size, and con-

formation to one he had packed so strenuously over obstacles. My impression was that this ant was making a fool of himself. Yet there are bacteriologists and, for that matter, many people in other callings just like my ant.

Nicolle did relatively few and simple experiments. But every time he did one, it was the result of long hours of intellectual incubation during which all possible variants had been considered and were allowed for in the final tests. Then he went straight to the point, without wasted motion. That was the method of Pasteur, as it has been of all the really great men of our calling, whose simple, conclusive experiments are a joy to those able to appreciate them. For there is an "art" of experimentation which is as elusive of definition as the art of colour, sound, or letters. Indeed, there is a Pegasus for science as there is for the arts, and he, like his mate, spreads his wings only when he feels on his flanks the thighs of one whom the gods have appointed to ride him.

In the case of the louse discovery, Nicolle had carried out no more than a half-dozen decisive experiments after years of observation of the disease and its epidemiology. In this instance, the experiments were easily confirmed. In some other matters his reputation was rather damaged than, otherwise by this habit of doing just enough work to convince himself and not carrying through far enough to convince himself and not carrying through far enough to convince others. He was one of the first, if not the first to assert—on the basis of a meagre experimental material—that epidemic influenza was a virus disease, and it was so described in French textbooks some ten years before the cultivation of the virus proved him right. Like other superb experimenters—Pasteur among them—he was always precise in his observations, but less interested in the theories bases upon them. Practically all the work he did was of an intensely practical nature, suggested by the problems he encountered in the field and at the bedside. Next to his typhus discoveries his greatest service was the determination of *infections inapparentes*, the fact that animals may contract many diseases and transmit them without showing any—or only very slight symptoms.

Apart from his scientific distinction, however, Nicolle was of the stuff of which the French Encyclopaedists were made.

I have seen his cultural scope approached only by a few Frenchmen and an occasional German of the old school—a type of learning that cannot be acquired by study alone, but represents the ripening of gifted minds that are attracted by everything about them worthy of interest

Nicolle was novelist, philosopher, and historian. His day began at 5 A M., when he sat down to write until seven-thirty. These were the hours that produced his essays and his prize novel. Then a frugal breakfast, and work in the laboratory until eleven. The heat then sent us to our rooms until three, a period of the day when the entire town of Tunis went to sleep, even the camels lay in the shade of hedges, and the wandering bands of Arabs rested near the wells, sleepily scratching themselves. Although, as far as the camels were concerned, the above is not strictly accurate. They are strange and—to a horseman—mysterious beasts. I have seen some of them in the suffocating heat of an African summer noon lie in the sun, not ten feet from the shade of a green hedge, eating a stick of wood with all signs of sybaritic enjoyment.

After three, we all worked again until seven, and in the evening we wandered out to Sidi-bu-Said or Carthage for dinner near the shore, with good food, passable Tunisian wine, and amiable conversation.

Those evenings linger in my mind as among the most happily peaceful I have spent. Either Nicolle chose his men with usual sagacity, or it just happened that he attracted kindred spirits. Burnet, now his successor, distinguished for studies on leprosy and Malta fever, was the author of a highly intelligent book of literary criticism. The entomologist was a poet, and one of the assistants a classicist who in his leisure hours was studying Roman archaeology. The conversation covered wide ranges from French literature to Arab architecture and Roman art. It is this wide scope of cultural interests in many people quite as competent as our own in their special fields which started me thinking about the superiority of the French and the former German secondary education over our own. I have met men, old and young, of these nations all over the world, and have often been impressed by the fact that, unlike most of our own compatriots of high specialistic learning, they showed signs of a richly cultivated intellectual subsoil.

At the officers' mess on a French auxiliary steamship, I once took part in a conversation which started with Diderot and Lamartine and then, through Bergson, passed on to William James, the second engineer and the perser locking horns on *Science vs Metaphysics*. A discussion of this kind would be unthinkable under similar circumstances among American or English sea-dogs, perhaps for the good of our naval services. However that may be, as conditions are now, I believe it is wise for an American specialist to conceal his extraneous interests until eventually they die of inanition, lest he be regarded as eccentric and incompetent.

Subsequently I saw Nicolle almost every year. We spent hours with his friend the Pere Delattre, head of the White Fathers and most learned on Carthaginian excavation. This old gentleman and his order again aroused in me that deep admiration for certain activities of the Catholic Church, to which I have been so often reluctantly constrained in spite of my utter lack of philosophical sympathy with its tenets. The White Fathers, so called from the Arab burnous which is their costume, are trained in the Carthage monastery and then sent to Equatoria, whence only a fraction of them ever return. Like their colleagues of the various orders I later met in China, they are keenly alive to medical problems and carry physical as well as spiritual comfort to the interior. Delattre himself was an urbane, learned, and kindly gentleman whose friendship alone was worth the journey.

In subsequent years Nicolle and I explored the historical corners of Paris and of Rouen together, and when separated we wrote to each other once every month. In Rouen he showed me the house of Corneille, the residence of Flaubert's father, surgeon to the Hotel Dieu, and a bawdyhouse that was installed in an ancient nunnery, which amused him greatly. We saw old Abbey where part of *Manon Lescaut* was written, and the garden pavilion on the Siene where *Madame Bovary* was created, a page or so a day. He introduced me to an old man who had known the Bovary's first husband, the apothecary, the one whose feet were always cold in bed, and to another who had a speaking acquaintance with Boule de Suif, for it appears that, to the town's consternation, both Flaubert and de Mau-passant took many of their characters from their neighbours in

regional lymph-nodes show considerable enlargement and together with the Primary Focus constitute what has been termed "The Primary Complex of Ranke" (1928)

In adults, we get the Adult Form or the so-called "post-primary form" of tuberculosis. Though originally described as being apical, the researches of Wessler and Jaches in 1923 and of Assmann in 1930 have proved the "sub-apical" or "infra-clavicular" site of this form of tuberculosis.

Every effort should be made to arrive at an early diagnosis of pulmonary tuberculosis, the sooner the disease is detected the greater the chance of ultimate recovery. An enquiry into the family history and past history of the individual may afford much useful information — (1) Constitutional factors play a big part in the genesis of tubercular disease. The importance of these factors in tuberculosis has been proved of late by the researches of von Diehl and von Verschuer on the development and course of the disease in twins. They have contrasted the similarity in the nature and course of tuberculous lesions in uniovular twins with the dissimilar nature and course of the disease in binovular twins. (2) An enquiry into the family history of the patient may by revealing a familial proclivity to the disease tip the scale in favour of this diagnosis or bring to light the existence of this disease in other members of the family. (3) History of exposure to infection. (4) History of tuberculous disease in the past, e.g. pleurisy with effusion or tuberculous lymphadenitis. Naegeli maintains, on the basis of considerable statistical study, that as many as 87 per cent of cases of apparently primary or idiopathic pleurisy with effusion between the ages of 18 and 30 are in point of fact tuberculous, in his opinion, lung-tuberculosis following on "wet pleurisy" always manifests itself within a period of three or four years. (5) Pathological conditions with a tendency to favour or prevent tuberculous disease of the lung should be enquired into; while silicosis, diabetes mellitus, lymphadenoma and portal cirrhosis are examples of diseases which favour the development of tuberculosis, anthracosis, mitral stenosis and high blood pressure belong to the opposite category of diseases that tend to prevent the development of the disease. (6) Age of the patient, tuberculous disease of childhood is entirely distinct from that of adults, Senile tuberculosis forms a distinct class with a high incidence of indurative lesions.

The so-called "stigmata of tuberculosis" have been the subject of much speculation and heresy in medical literature Hippocrates, the father of medicine, as far back as 500 B C described a "habitus phthisicus" and believed in the susceptibility of the "blond-haired and blue-eyed type" of individual to tuberculosis According to Burton Wood, the face of a tuberculous patient (Facies Tuberculosa) recalls that from an Elizabethan Love Lyric In Fishberg's opinion, the most characteristic feature of a consumptive patient are his eyes, he describes them as "deeply set in large sockets" "with a characteristic brilliancy", "transparent, lustrous, bright, dimly brilliant" The so-called "hectic flush" of tuberculosis is seldom encountered in India except in the acute forms and in the preterminal phases of the chronic forms

The "leptosomous" or "hyposthenic" form of body build has been regarded for years as being more prone to tuberculous disease than the "pycnic" or "hypersthenic" build This universally accepted fact has been questioned of late by certain European authors on the basis of their work on "the development of tuberculosis" in twins The "phthisical form" of chest (comprising of the "flat" and "alar" forms) is familiar to us all

No description of the consumptive can be considered complete without a reference to the classical "spes phthisica" or euphoria of the individual It is as if Mother Nature compensates the patient for his physical suffering by endowing him with an undue amount of optimism or mental cheerfulness, there is "hope to the very last" Burton Wood refers to this aspect of the tuberculous mind as an "ostrich complex", the patient just burying his head in the ground and not facing facts as they stand

In the case of Pulmonary Tuberculosis, more than in any other disease, a Delay in Diagnosis spells Danger, nay even Death It is therefore our duty to exert every possible and use every method known, clinical or instrumental, in order to detect the disease in its early or incipient phases Subjective manifestations of tuberculosis usually owe their origin to one of two factors (1) general or toxic effects of the tuberculous toxin (Tuberculo-toxic symptoms) (2) Effects of local disease in the lung

The usual type of onset in pulmonary tuberculosis (classical onset or insidious onset) is familiar to us all, there is cough, with

fever, loss of weight, loss of appetite and sweating, such a clinical picture suggests the possibility of tuberculosis even to a layman. It is to the lesser known forms of clinical onset of tuberculosis that I wish to direct your attention today. (1) There is the so-called *gastro-intestinal form* of onset, where symptoms are mainly referred to the stomach in the early stages. Because of symptoms like anorexia, inability to digest food, flatulence, constipation or diarrhoea, the patient has been diagnosed and even treated for an imaginary "gastritis", "acidity", "indigestion" or "weak stomach". (2) The *neuresthenic type* of onset deserves more attention from the medical profession than it gets at the present time. The early case of tuberculosis is sometimes listless, irritable and morose, as a result, his symptoms are erroneously put down to Neuresthenia or Hypochondriasis, the poor patient is fed on Bromides and Valerian till the appearance of fever, sweating or persistent cough draws the attention of the attending physician to the disease in the lung. The lesson we learn from such a case is never to label a patient's complaint as hysterical, functional or psychological unless organic disease has been convincingly excluded by a thorough examination. (3) The *catarrhal or Influenzal type* of onset may present a difficult diagnostic problem. The patient suffers from repeated attacks of typical influenza, common cold or bronchitis before the classical symptoms and signs of tuberculosis manifest themselves. I can recall the instances of two English women, both admitted to Hospital under similar circumstances in London, in each case, there had been three or four attacks of typical "flu" within a period of five or six weeks before admission, the small area of infiltration in either case was revealed by a routine fluoroscopic examination. (4) The *asthmatic type* of onset is frequently missed. The young patient, usually in her twenties, begins to experience typical attacks of so-called "bronchial asthma" for the first time, physical examination of the chest discloses typical signs of asthma, viz prolonged expiration, rhonchi and crepitations, in the majority of such cases, the patient has been actually treated for asthma for months before the lung-infiltration is discovered. It is not clear how this early tuberculous infiltration induces asthmatic attacks, whether this occurs through the agency of a nervous reflex mechanism or through the absorption of the tuberculo-toxin, it is difficult to say. Within the past three months, I have come across two such cases of tuberculosis with the asthmatic

type of onset (5) The *pneumonic type* of onset is fortunately familiar to most clinicians. It is practically confined to the acute form of tuberculosis, which is variously referred to as Caseous Pneumonia, Pneumonic Tuberculosis or "galloping consumption". For the first few days of illness, the clinical course is in no way different from that of lobar pneumonia, suspicion is only aroused when the temperature fails to come down to normal at the usual time or when it takes on a "hectic", swinging or intermittent character or when the customary leucocytosis of lobar pneumonia is lacking. The diagnosis of Caseous Pneumonia is finally clinched by the demonstration of tubercle bacilli in the sputum in addition to a low white cell count in the blood. (6) In hospital practice we frequently come across the *malarial type* of onset, the patient who gives a history of fever with rigors is immediately put on a quinine mixture or given injections of quinine, when he fails to respond to the drug the dispenser is sometimes blamed for not having dispensed the mixture properly, routine fluoroscopy discloses the true "culprit" in the nature of a tuberculous infiltration. (7) Many cases of lung-tuberculosis are admitted to hospital as cases of "severe anaemia" and saturated with Iron Mixtures until the incriminating focus is finally discovered. (8) Amenorrhoea (and at times, dysmenorrhoea) arising in a patient with previously normal and regular "periods" should prompt a careful examination of the chest for possible lung disease, in a fair percentage of cases of tuberculosis in young women, the first or presenting symptom of tuberculous disease is hypomenorrhoea or amenorrhoea. (9) Hoarseness of voice is occasionally the first or presenting symptom in cases of pulmonary tuberculosis. It is due to associated tuberculous laryngitis. In practically all such cases, the primary focus is in the lungs and not in the larynx, a careful radiological examination practically always discloses a primary tuberculous infiltration in the lung in so-called cases of Primary Tuberculosis Laryngitis. (10) Pleuritic onset, Dry pleurisy, pleurisy with effusion or spontaneous pneumothorax may usher in an otherwise typical case of pulmonary tuberculosis. (11) Haemoptysis is frequently the presenting sign in cases of tuberculosis. (12) The "latent" or *asymptomatic form* of onset. The presence of a tuberculous infiltration is sometimes discovered by accident. Tuberculous foci are sometimes discovered during routine medical inspection of students in schools and colleges. A "warm hand-shake," a "run down look" or

a slight cough noticed by friends or relatives may lead to the discovery of the hidden focus

A few words about the important symptoms of tuberculosis may not be out of place at this stage. (1) *Cough* Almost invariably present and frequently the leading symptom, the cough of pulmonary tuberculosis presents no pathognomonic features, it is in no way distinct from the cough of other respiratory and non-respiratory diseases. The cough of tuberculosis is often confined to the morning hours in the early phases of the disease, in the later stages, it becomes continuous and intractable. It is more often diurnal than nocturnal, a point of some diagnostic value. It is frequently provoked in the early stages, by talking, by deep breathing or by the inhalation of foreign substances. It may or may not be associated with expectoration, in the early stages of the disease it tends to be dry. It is often resistant to simple cough remedies. A useful rule to remember in practice is Never dismiss lightly a cough that has persisted for a month or more in spite of medical treatment.

The cough of pulmonary tuberculosis may be mistaken in the early stages for a nervous cough, a "smoker's cough", a "stomach cough" or the cough associated with infection in the upper respiratory passages, confusion may arise between the cough of tuberculosis and the cough associated with insufficiency of the left ventricle of the heart and secondary to pulmonary congestion. In children a persistent and dry cough may be due to Bronchial Lymphadenopathy.

The French have described a so-called "Emetic cough" or "Toux emetisante" in the early stages of pulmonary tuberculosis; half an hour or so after meals, a tickling sensation is experienced at the back of the throat and the contents of the stomach are forcibly ejected without a sense of nausea.

It is worth while remembering that in cases of early tuberculous infiltration, there may be a complete absence of cough.

(2) *Fever or Pyrexia* The great majority of cases of pulmonary tuberculosis are febrile. In fact, Fishberg goes far enough to insist that "tuberculosis if active is never afebrile" and denies the existence of the so-called "afebrile cases" described by other authors. Such a divergence of opinion is due to the fact that the rise of temperature in early or incipient cases of tuber-

culosis tends to be transitory and may appear for an hour or two only during the entire day. In order not to miss such transitory rises of temperature, attention is directed to the following features (i) Have the body-temperature (preferably rectal) recorded and plotted on a temperature-chart every two hours of the day. The most likely time for a transitory rise of temperature in tuberculosis is around 6 p m., in the evening (ii) Make a note of the "diurnal variation" of temperature, i.e. the difference between the highest and lowest temperature readings of the day. In tuberculosis there is a diurnal variation of more than 2 degrees (Daremborg, 1905) (iii) The "provoked fever test" or "exercise test" ("fièvre provoquée de Daremborg") may prove extremely helpful in doubtful cases. After a standard exercise (e.g. a walk of two miles) there is normally a slight rise of temperature, not exceeding 1 F., that returns to normal within half to one hour. In early tuberculosis, on the other hand, this rise of temperature exceeds 2 F. and the fall to normal takes two hours or more.

(3) *Tachycardia* A rapid pulse, continuous or paroxysmal, in a young person who is losing weight, coughing or feeling poorly, should suggest the possibility of tuberculous infection. Tachycardia is a characteristic feature of tuberculosis observed in all its stages. In Fishberg's opinion, more than 90 per cent of incipient cases of tuberculosis have a pulse-rate out of proportion to the body-temperature.

(4) *Sweating* It is well to remember that "profuse sweats" are not by any means, pathognomonic of pulmonary tuberculosis, they are frequently encountered in cases of malaria, liver-abscess and conditions of suppuration in the body. In children, they suggest vitamin D deficiency or Rickets. The sweats of pulmonary tuberculosis tend to occur in the early hours of the morning, round about 3 a.m. The patient may be quite oblivious to the presence of "night sweats" even in the most advanced of cases.

(5) *Loss of weight or wasting* has been recognized by the medical profession for generations as a classical sign of lung-tuberculosis, as a matter of fact, the word Phthisis means wasting. The lay public is so familiar with this aspect of the disease, that any failure to gain weight in a child or relative is immediately ascribed to a tuberculous tendency and the patient taken

from doctor to doctor for a thorough investigation of the "weak chest" Some doctors who are at a loss to explain this loss of weight, promptly accuse the poor patient of "evil habits" or masturbation, such an attitude is thoroughly unjustified and may prove disastrous to the mental balance of the individual It is worth while bearing in mind that during and after puberty, there is a state of endocrine imbalance in the body which may lead to a gain or loss in weight, such a fluctuation in weight is usually transitory

(6) A sensation of "slow heat" or "burning" in the body, especially in the bones of the extremities, is so commonly complained of by patients with tuberculosis, that I have come to regard it as a symptom of some diagnostic import A similar symptom of "burning" may be encountered in cases of malaria, pneumonia and other fevers, but in such cases it is more marked as a rule in the head and trunk than in the extremities and is usually of a more intense nature, not conforming to the description of "slow heat"

There is an unfortunate tendency at the present time, on the part of the medical profession, to underrate the value of proper physical examination of the patient, in the detection of early tuberculous disease Roentgenographic and laboratory investigations are becoming increasingly popular Such an attitude is perhaps justified in a modern European city with all its facilities and equipments, but in a country like India, where the majority of hospitals are devoid of even a small X-ray plant, we cannot afford to entertain any such idea We are of necessity obliged to fall back upon the age-old methods of physical examination and there is no doubt that with practice one can derive an immense amount of information from the use of these methods

The trouble with text-books is they limit themselves to a description of the full-blown case of pulmonary tuberculosis with all the signs of cavitation, fibrosis, consolidation etc Little or no attempt is made to describe the clinical picture of early or incipient tuberculosis, the only form of tuberculosis that offers any hope of therapeutic success A correct diagnosis of the disease should be made long before the patient develops its various classical signs and attains the status of a "museum-specimen"

A careful *inspection* of the chest is imperative in every case, it yields much useful information and may even clinch the diagnosis. Local areas of retraction and deficient movement are found in the later stages of the disease only. We should direct our attention to early signs. (1) Even in early cases, aprominence of Mohrenheim's fossa (or infraclavicular fossa) is usually detectable, the small triangular depression bounded by the clavicle, deltoid and pectoralis major muscles increases in depth and size on the affected side. (2) Dalmegé's Sign some degree of flattening of the Deltoid muscle on the affected side may be obvious. (3) The mammary gland on the side of disease may appear smaller than its counterpart on the opposite side. However, in a case of right-sided pulmonary tuberculosis recently seen at the K E M Hospital, it was the left breast that appeared small and shrunken. (4) A diminution or delay in the movement of the chest on the affected side. Careful inspection of the chest from various angles (especially downward inspection from above the head of the patient) practically always reveals some abnormality of movement. In early cases, we find either an actual diminution in the range of movement of the chest on the affected side or what is equally important a "delay" or "lag" in the commencement of movement on that side. The "lag" in movement may be secondary either to the actual lesion in the lung or to an alteration in the tone of the over-lying muscles.

Palpation (1) helps to confirm the diminution or "lag" of movement on the affected side, as detected on inspection. (2) Pottenger's Sign is of questionable value, Pottenger described an increase in the quality of resistance experienced by the examiner's hand on light palpation of the apical area on the affected side, in early cases, with progress of the disease, this rigidity on palpation is said to diminish to a threshold below that of the sound lung. In this connection, it might be noted that John Guy has described in early cases of tuberculosis a spasm, hardness or increase of tone in the superjacent muscles. (3) Vocal fremitus may or may not show an increase in early cases. States of consolidation of lung-tissue are always associated with an increase in fremitus, with the following exceptions (a) when there is pleural thickening associated, (b) when there is an associated bronchial stenosis, (c) when consolidation is patchy and deep-seated, and (d) when there is an associated pneumothorax. Before

attaching a pathological significance to alterations in fremitus, it is necessary to exclude the normal or physiological difference of fremitus on the two sides (4) A sign of great importance to my mind is "deviation of the trachea" to one or other side as determined by palpitation of the trachea in the neck, between the clavicular heads of the Sterno-cleido-muscles on the two sides Deviation of the trachea may direct our attention not only to the presence of disease but also to the site and nature of the disease-process, e g, fibrosis at the right apex

Percussion

In the opinion of James Maxwell, percussion is the least valuable and potentially the most misleading of all the methods of physical examination Since the discovery of percussion by Leopold Auenbrugger of Austria, the value of this method of examination has been questioned from time to time The tendency at the present day is to regard percussion as "a rather overrated aid to diagnosis" There is no doubt that indiscriminate or hasty interpretation of percussion signs may let down the offending physician very badly indeed I would like to direct your attention to the following points (1) For the detection of early tuberculous disease, a very light stroke is essential, a heavy stroke, by setting up vibrations in adjacent normal lung-tissue, will tend to dampen or modify the "sound" of disease (2) In pulmonary tuberculosis, extra attention should be paid to the percussion of apical areas, this may be conveniently carried out by percussing from above the patient, with the latter sitting on a low stool It is of historical interest to know that percussional alterations at the apices in cases of tuberculosis were described as early as 1830 by Laennec, who also described similar signs in the interscapular region (3) Normally, the loudest and most resonant note is found in the 2nd and 3rd intercostal spaces on the right side, an important rule to remember is that normally, the right side of the chest (apical) is more resonant than the left and the infra-clavicular region is the site of maximum resonance (4) Extraneous factors are frequently responsible for abnormal signs on percussion, in this connection, particular attention is directed to the presence of a scoliotic deformity of the chest, the presence of a cervical or supernumerary rib on one side and unequal or assymetrical development of the muscles of the chest-wall (5) Impairment of percussion-note at the apex

does not necessarily signify tuberculous infiltration, it may also be caused by apical pneumonia, apical pleurisy or by an area of atelectasis at the apex secondary to bronchial obstruction in the hilar region (6) Percussion is of no value in distinguishing recent or active infiltration from old or quiescent tuberculous disease

The importance of apical percussion in the diagnosis of tuberculous disease has led several authorities into proposing newer and better methods of percussion (1) Kronig's Method With the advance of radiology, Kronig's method of mapping out apical zones of resonance is being gradually discarded With good technique and sufficient experience this method is capable of furnishing considerable information regarding the site and extent of disease in tuberculous cases At the apex, on either side, a strip or band of resonance (Kronig's area or Isthmus) normally connects the anterior and posterior areas of lung resonance, Kronig's isthmus is normally three-finger breaths wide on the right and two finger-breaths wide on the left side Unilateral diminution or shrinkage of this band of resonance or "blurring" of one or both margins of this band suggests presence of disease on that side (2) John Guy's Method of Transmitted Percussion This is a modification of Kronig's method, where auscultation is combined with percussion (Auscultatory Percussion) After arranging the chest-piece of the stethoscope over the 2nd intercostal space in front, Kronig's areas of resonance are mapped out by noting with the aid of the stethoscope alterations in the character of sounds (3) Plesch has suggested a modification of the pleximeter for the purposes of apical percussion, he advocates the use of a "hooked-finger" or "finger flexed at right angles" instead of a straight finger as in the normal course of events, by this modification he claims to have made the localization of early infiltrates easier (4) The method of Tidal Movement Kronig's bands of resonance normally show variations in size and shape with respiratory phases, the absence of this phenomenon on one side affords evidence of disease on that side

Two other signs both dependent on percussion, which have been recommended for the detection of early apical disease are (1) Roussel's Sign Pain on light percussion over the infra-clavi-

cular region, as far down as the 4th rib (2) Abraham's Sign Impairment of note (from dull to flat) over the acromian process

• Auscultation

This may furnish evidence of early tuberculous disease in one of two ways (1) by a modification or change in the nature of breath-sounds, or (2) by the appearance of adventitious or anomalous sounds, e g, rales, crepitations, and "rub"

In early cases of pulmonary tuberculosis, look particularly for the following modifications in breath-sounds (1) Diminution of air-entry or weakening of the respiratory murmur (2) Puerrile breathing or prolonged expiration (sometimes referred to as Jackson's Sign) (3) Harsh breathing harsh and high-pitched inspiratory sound with prolongation of expiration (4) Cog-wheel, jerky or interrupted breathing (the so-called "respiration saccade" of French authors) The normally continuous inspiratory sound becomes jerky, disjointed or broken up (5) Granular breathing of Grancher The inspiratory sound becomes "coarse", "rough" or irregular There has been much conflict of opinion as to which of the above-mentioned alterations in breath-sounds occurs first in tuberculous disease Judging from a review of modern text-books on tuberculosis, the two most likely alterations are (i) "diminution of air-entry and (ii) "harsh breathing" Forms of breathing, referred to as "bronchial" and "Broncho-vesicular", are not met with in early cases as a rule, they denote extension of the disease-process To facilitate the detection of minor alterations of breath-sounds, Grancher has advocated the method of "single phase auscultation", where each phase of respiration is independently auscultated

Adventitious sounds Of these, *crepitations* comes first in order of appearance and importance In early stages, we get fine crepitations or "crepitant rales" at one apex, these crepitations are somewhat characteristic, (i) they are persistent, (ii) they tend to occur at the end of inspiration (iii) they are found most often, anteriorly, just below the clavicle and posteriorly, in the neighbourhood of the scapular spine in the so-called "Alarm zone of Chauvet" (iv) they are frequently provoked by coughing or by breathing deeply With each respiratory cycle there may appear either a whole "shower" of crepitations or what is much less common, a "single" or "isolated" crepitation (the so-called "clicking rale")

Crepitations of tuberculosis have been ascribed to a variety of causes (i) separation of sticky, alveolar surfaces by the inspiratory current of air, (ii) sounds produced by friction of tubercle-laden pleural surfaces, (iii) due to patchy atelectasis

There is a tendency on the part of certain clinicians to doubt the existence of tuberculosis in the absence of crepitations, such an attitude is unjustified and may prove disastrous because crepitations or rales, which are due to softening of caseous matter, may be entirely missing in the early stages Fishberg goes so far as to assert that to wait for the appearance of rales is worse than waiting for the appearance of tubercle bacilli in the sputum

Tuberculous rales may present difficulties in diagnosis, especially from the following conditions (1) Atelectatic or marginal rales, so frequently observed along the anterior and lower margins of the lungs in individuals who breathe "superficially", they are due to "unfolding of collapsed alveoli" and tend to disappear after a few good breaths Burghart has described in cases of early apical tuberculosis, fine crepitations along the anterior inferior margin of the affected lung (Burghart's Sign), whether Burghart's crepitations are merely atelectatic rales or constitute a distinct entity, it is difficult to say, I am inclined to view the former view as correct (2) From "old, healed or quiescent" foci of tuberculosis at the apex There is a tendency for these old foci to develop a mild degree of bronchiectasis (local), which may give rise to cracks or rales during or after infections of the respiratory passages (Naegeli) (3) From the crepitations of apical pneumonia or the "pleural crepitations" of apical pleurisy (4) From the crepitations of pulmonary congestion, such as results from left ventricular failure (5) From "muscular sounds" or "spurious rales" due to contractions of the Trapezius and other muscles, they can be made to disappear by relaxing the muscle or muscles in question

With progress of the disease, fine crepitations are replaced by coarse and bubbling rales

A persistent unilateral apical rhonchus is suggestive of tuberculous infiltration A pleural "rub" may be audible at the apex in cases of pulmonary tuberculosis, it is usually indicative of a focus in the vicinity of the visceral pleura

There are two fairly common conditions which present considerable difficulty in diagnosis, from the point of view of physical signs, unless the physician bears these conditions in mind, he is likely to miss them. First, I wish to refer to the condition known as "*accessory lobe of the azygos vein*", which may present a diagnostic problem to the unwary. In this condition the Vena Azygos Major takes an anomalous course, intending the apex of the right lung. Clinically, one may find at the right apex, impairment of percussion note, alteration in the character of breath-sounds and the presence of crepitations. Diagnosis is usually clinched by the demonstration of the pathognomonic "*common-shaped shadow*" in the skiagram.

The second diagnostic bugbear, I wish to refer to, is a condition of *displacement or pulling of the trachea to one side* as a result of indurative or fibrotic disease of the lung on that side. Clinical examination, in such cases, reveals the presence of bronchial breathing, increased vocal fremitus, bronchophony and whispering pectoriloquy over one apex (usually the right). More often than not, an erroneous diagnosis of "*apical cavitation*" is made by the physician in attendance. Fluoroscopic examination offers a terrific shock to the physician, who finds, instead of a cavity, merely indurative or fibrotic disease at the apex, the signs of cavitation are due to a grossly displaced trachea. The importance of this syndrome as a diagnostic problem was brought to my notice for the first time at St. Thomas's Hospital in London, when a case diagnosed by me as a typical case of "*apical cavitation*" turned out on x-ray examination to be of this nature. Since that time, I have come across two more cases of these type, once at the J. J. Hospital and once at the K. E. M. Hospital, Bombay. In each case, the house-physician had diagnosed cavitation at the right apex. On the basis of a palpable displacement of the trachea to the right, the possibility of the "*displaced trachea syndrome*" was suggested by me and later confirmed by the taking of skiagrams.

X-Ray Diagnosis of Pulmonary Tuberculosis

According to many present-day authorities too much reliance has been placed in the past on physical signs, as aids to diagnosis, the methods of percussion and auscultation have

been grossly overrated. The universal adoption of radiological methods has brought to light definite tuberculosis foci and infiltrations in cases which have never been suspected clinically of tuberculosis disease. There is no doubt that radiology detects the presence of early or incipient tuberculosis with greater certainty than any other method known, that is the opinion of Twining, Assmann, Samson, Brown and many others. However, in a country like India, where radiological facilities are not generally available, the physician is obliged to fall back upon the age-old methods of physical examination for his diagnosis.

Radiology presents certain definite advantages over clinical methods of examination. (1) It is more successful in the detection of early disease and may reveal even extensive tuberculous infiltrates in cases where no disease has been suspected clinically. This is particularly so in the case of 1 Early sub-apical infiltrates, 2 deep-seated para-hilar lesions and 3 in tuberculous lesions along the interlobar septa. In a series of over a thousand cases investigated by Samson and Brown, as many as 396 cases pronounced normal clinically showed tuberculous lesions on radiological examination, on the other hand, in not a single case of clinically diagnosed tuberculosis was a normal skiagram reported. (2) It determines the exact location and extent of the disease process, as a rule, radiology reveals much more extensive disease than suggested by clinical methods of examination. (3) It helps to differentiate tuberculous disease from other diseases with similar symptoms and signs, e.g. pulmonary congestion, lobar pneumonia and displacement of trachea.

In order to get the best results, clinical and radiological methods should be used in conjunction. Sole reliance on one or other method is likely to let the physician down very badly. Mistakes in diagnosis may occur even with the most highly developed of radiological techniques.

1 Occasionally, when radiology reveals nothing abnormal in the lung, clinical methods leave no doubts to the existence of tuberculous disease, I have observed two cases, where, in spite of a cough, signs of apical tuberculosis and positive sputum report, the radiologist's report was negative. Such a

discrepancy is likely to arise if the lesion is very small or situated behind a rib-shadow.

2 Radiology is of no value in distinguishing active from quiescent tuberculous disease

3. Lung-shadows or opacities seen in skiagrams are seldom specific, similar shadows may be noted in cases of lung-carcinoma, lobar pneumonia etc

The success of radiology has prompted certain authorities to urge the necessity of undertaking "mass radiological investigations" in certain classes of society, especially in nurses, medical students and inmates of tuberculous institutions Twining recommends the freer use of radiology as an essential part in the fight against tuberculosis

For a proper interpretation of chest skiagrams in cases of tuberculosis, a thorough knowledge of "the sites of predilection" is essential Early infiltrates are particularly prone to arise at the following sites (i) the sub-apical or sub-clavicular region of the lung, especially of the right lung, this is the "site of choice" (ii) apices of the right and left lower lobes (iii) the lingual tip of the left upper lobe (iv) the base of the right upper lobe

For a proper interpretation of lung shadows, it is necessary to subject the patient to a fluoroscopic examination in addition to the taking of a skiagram Fluoroscopy will not only show the presence of infiltrations but will also demonstrate the normal phenomenon of "clearing of the lung-parenchyma" coincident with inspiration Small shadows, obscure infiltrations, cavities with fine walls and the "snow-storm appearance" of military tuberculosis, conditions likely to be missed during fluoroscopy come out well on an x-ray plate

For the early detection and localization of lung-shadows, special methods of radiography have been devised of late, e.g Tomography, Kymography and Stereoscopic radiography For a proper visualization of the apices, Twining has suggested the use of the "lateral stoop position"

So-called "peri-bronchial tuberculosis" and "hilm tuberculosis" which were frequently diagnosed in the past from x-ray appearances, have now fallen into disfavour, their very existence

is questioned by present-day radiologists who refer to them as "relics of the past generation "

Examination of Sputum

In every case of pulmonary tuberculosis, suspected or obvious, incipient or advanced, repeated and pains-taking examination of the sputum for tubercle bacilli is essential for a proper diagnosis, follow-up and treatment of the case. A stained slide of sputum (Ziehl-Neelson Method) needs a minimum scrutiny of half-an-hour under the microscope, before it can be pronounced "negative", in a case suspected of tuberculous disease, a definitely negative report on the sputum cannot justifiably be given until the sputum has been found repeatedly negative on at least six different occasions. Cases have been reported where the persevering physician has been rewarded by a positive report after as many as twenty futile attempts (Maxwell). To ensure reliability in sputum examinations, one must insist on a correct technique, a careful scrutiny and repeated observations. Contamination of sputum with acid-fast organisms may arise occasionally from extraneous source, e g, from tap-water or dirty test-tubes.

The presence of tubercle bacilli in the sputum proves the existence of a pulmonary lesion in something like 98 per cent of cases, in the remaining 2 per cent, there is isolated tuberculous disease in the tonsils, larynx, pharynx or bronchial lymph-glands. Even with extensive tuberculous disease of lung-tissue, tubercle bacilli may fail to appear in the sputum, this is particularly so in cases of (i) miliary tuberculosis, where haematogenous dissemination is the rule, (ii) in the early stages of caseous or tuberculous pneumonia, where the bacilli may be enmeshed within a mass of pneumonic exudate, and (iii) at times, in chronic forms of lung tuberculosis, in the so-called "closed cases "

Considerable difficulty may be encountered in obtaining sputum for examination, especially in the case of children who instead of coughing up sputum tend to swallow it, this childhood habit may persist in some cases to adult life. In case of difficulty the following alternative measures are suggested (1) Collection of sputum after the administration of expectorants by mouth, a combination of ammonium carbonate and potassium iodide proves effective in many cases where the patient finds difficulty in

bringing up sputum (2) Cohen and Burton Wood have devised an ingenious "laryngeal mirror method" in order to circumvent this difficulty. A laryngeal mirror is adjusted in the position customary for indirect laryngoscopy and the patient instructed to cough, by this method the mirror gets sprayed with sputum directly from the air-passages (3) Examination of washings from the stomach, obtained with the aid of Ryle's tube, for the presence of tubercle bacilli (4) Examination of faecal matter for the presence of tubercle bacilli

An intelligent interpretation of the *Blood Count* in cases of pulmonary tuberculosis, may yield much useful information. This subject has been reviewed exhaustively by Oatway (1934). I will try to summarize our present-day views on the subject of blood counts in cases of lung tuberculosis (1) In the acute forms of tuberculosis, including the miliary form of tuberculosis, we find a leucopenia, a reduction in the platelet count and a progressively increasing hypochromic anaemia (2) Signs of good prognostic import are 1 a lymphocytosis, absolute or relative, and 2 A normal eosinophil count (3) Signs of bad prognostic import are 1 a lymphopenia, 2 a diminution or disappearance from the blood of eosinophil cells, and 3 a leucocytosis with preponderance of polymorphonuclear cells, especially of "young or immature forms" (4) There is a rise of platelet count during the "active" and a fall during the "healing" or "quiescent" phases of the disease, Bannerman (1924) has made use of this observation in the determination of prognosis (5) The "monocyte lymphocyte ratio" has been investigated in the tuberculosis of both man and animals. This ratio, normally about 1 : 3 becomes 1 : 4 or more in favourable and 1 : 1 or less in unfavourable cases

The finding of an increased *Sedimentation Rate*, though by no means diagnostic of tuberculosis, certainly tips the scale in favour of that disease in doubtful cases. It is more useful for the purposes of follow-up. In the opinion of Naegeli, a "determination of the serum globulin" affords more reliable information than a determination of the rate of sedimentation of red cells, the latter is more likely to be influenced by extraneous factors

The *Tuberculin Test*, hailed at one time as a discovery of great moment, has lately been falling out of favour with the medical profession. It has too many drawbacks (1) A "positive result" is obtained even with old, quiescent and completely

fibrosed tuberculous lesions, as a result, the patient may erroneously be looked upon as tuberculous and even treated as such (2) A "positive result" is obtained in 95 per cent of normal adolescents (Naegeli) and in 90 per cent of individuals after puberty (Aschoff), hence, a positive result is of little or no value in adults (3) In the presence of a super-added secondary infection, a previously "positive" test may become "negative" in spite of there being extensive tuberculous disease (4) In the opinion of Selter, the tuberculin test can not be considered specific

The tuberculin test may prove of value in the following types of cases (1) in children, where a "positive" reaction may direct attention to a primary tuberculous focus, and (11) in grave or unfavourable cases with failing bodily resistance, where a previously "positive" reaction may become "negative"

Certain modifications of the tuberculin test have been suggested and given extensive trials in European countries (1) Attempts have been made to induce "focal reactions" in diseased lungs by injecting tuberculin in large doses, evidence of a "focal reaction" is furnished by a change in physical signs over the affected lung or by the appearance of fresh rales This test may prove dangerous or even fatal, by reactivating latent foci of tuberculous disease (2) D'Amato's Test In a person suspected of being tuberculous, d'Amato injects subcutaneously one-millionth of a milligram of tuberculin, a white cell count is carried out at intervals of half-an-hour for three hours or more The development of a definite leucopenia constitutes a positive reaction This test has been tried extensively in Italy, with promising results

One can reiterate over and over again that to get any therapeutic success with a disease like pulmonary tuberculosis, an early diagnosis is essential In the case of acute forms of tuberculosis as well as in the advanced chronic forms, there is little one can do in the way of treatment Is it in any way surprising then, if the layman, through centuries of experience, has come to regard this disease as the most prevalent, progressive, the most relentlessly brutal and the most deadly of diseases?—A disease, which with the cruel precision of a Delilah saps the poor victim dry of every ounce of strength and vitality, robs him of his very life-blood, until, reduced to mere skin and bone he craves for merciful release

Analytical Review

PREVENTION OF DIABETES MELLITUS

By

C. C. MERCHANT

M D P S

(From *The Pharmacological Dept., Seth G S Med College, Bombay*)

(Continued from the last issue, p 259)

Difficulties in the Anti-Diabetic Campaign

From amidst the welter of innumerable etiological factors just considered above, it is very difficult or rather impossible to pick out any one or more conditions to which the development or onset of diabetes may directly or indirectly be ascribed with any degree of certainty. The etiology of diabetes still remains elusive and more a matter of suppositions and theories. For this reason it is considered almost impracticable to achieve absolute prevention of the disease with any reasonable measure of success. No serum, vaccine or chemotherapeutic agent has yet been prepared or even thought of, which would confer immunity against diabetes for however a shorter time it may be, nor is it considered feasible to stamp out diabetes or check its incidence by means of sanitary reforms or public health measures as in the case of malaria, typhoid or small-pox.

Diabetes an Incurable Disease?

The experience gained in Europe and America where anti-diabetic campaigns have already been launched, has been very encouraging and teaches us that "greater the number of urine and blood examinations performed, greater the number of families examined, and greater the number of patients put under treatment, greater are the chances of bringing the disease under rapid and complete control." At present, the best hopes for immediate and substantial reduction in the number of diabetic deaths and eventual conquest of the disease centre round early detection combined with prompt and prolonged treatment of the disease—at a stage when the symptoms are almost inconspicuous or extremely mild. A great hindrance to success in the fight against diabetes is the idea that has been firmly rooted in the minds of the public as well as those of a large number of orthodox medical practitioners that "diabetes is an incurable disease" and no form of treatment, dietetic or medicinal perhaps with the exception of total or partial restriction of sugars, is ever likely to arrest or check the progress of diabetes. This belief—a legacy of the

past generations when very little was known about the physio-pathology of diabetes and when Insulin was yet to be discovered—is the cause of much misery and ill health, and requires to be soon dispelled. The reason why it still exists is perhaps accounted for by the supposed failure of a larger section of the medical profession—particularly the general practitioners, to appreciate the practical importance of the newer knowledge in the physiopathology of diabetes acquired during recent years. They should be able to discern between what is new and valuable and what is new but spurious.

Lack of Specialized Treatment

There is enough evidence clinical as well as experimental that diabetes, though it may not be a curable disease, is not unconquerable. To-day, if a diabetic would co-operate with his medical adviser and observe a few simple hygienic rules specially relating to the life of a diabetic, he can hope not only to live long but also to live a life as normal and active as a non-diabetic person.

Another, not an insignificant difficulty in the way of successfully fighting diabetes is the fact that the present day treatment of diabetes requires specialized skill and knowledge as in the treatment of tuberculosis or a venereal disease, and also hospitalization of the patient at least in the beginning of treatment and during complications. At present, not one big city of India including Bombay the "Urbus Prima in Indis" can boast of a special hospital or even a special ward in general hospital to receive and treat diabetic patients. Moreover on account of comparatively restricted accommodation, acute cases are often refused admission or have to wait for some time before they are admitted. Facilities in out-patient departments are equally restricted and very few diabetics are able to receive proper and adequate attention and treatment.

Ignorance and Apathy of the Public

Last of all, poor economic condition, illiteracy, general ignorance and apathetic attitude of a larger proportion of the population towards matter of health, combined with unfounded biases and prejudices against newer and more scientific forms of treatment are matters which greatly hamper the progress towards eradicating the disease from the community, and will have to be overcome by means of education and active propaganda before fruitful results can eventually be achieved.

Diabetes—a Public Health Problem

Diabetes has, until very recently, received very little or no attention at the hands of the public health authorities, as so far nothing has been known of any way on the part of the community or public health bodies which will diminish the liability of an individual to contract diabetes nor has the diabetic patient been known to communicate his disease to his neighbours nor to prove a nuisance to them by virtue of his disease. However Dr Charles F Boldau

(Lancet P 566, 5-3-38) views diabetes as being an important public health problem. He argues that "modern treatment can improve and prolong the lives of diabetics, it is for the public health authorities to aim at getting the largest possible number of diabetics recognized and treated", and quotes the convincingly good results achieved by the Diabetic Association (founded in 1934) of New York within a comparatively short time of its existence. The fact that diabetes is an important public health problem has been recognized in England and has led to the foundation of the "Diabetic Association" in London (1935) with very wide aims and objects on its programme.

Anti-Diabetic Campaign

Considering the widespread distribution of diabetes in India and the general apathetic attitude and ignorance of its people, the urgent need for a properly organized campaign on a nation-wide scale cannot but be overemphasized. The first step in the anti-diabetic campaign would be the formation of organizations or associations in all the important cities and towns of India which all should be affiliated or act as branches of a central or parent body or organization which would be situated in one of the main cities like Bombay, Madras, Calcutta or Delhi. The cities are generally best suited for waging the fight against diabetes since they are by definition, areas of concentrated population, and people can be reached most easily and with comparatively less expense for the purpose of propaganda, diagnosis and treatment. Later, the activities should be extended to smaller towns and villages by opening of smaller centres.

Programme

The immediate programme of these organizations would be in short (1) To provide in their areas increased facilities for the diagnosis and treatment of diabetes (a) by stimulating existing hospitals and clinics to take more interest in diabetes and encouraging their co-operation and (b) by opening a number of clinics at different suitable places with attached health visitors and providing wherever possible special hospitals or special wards in general hospitals for receiving increasing number of diabetic patients, with special facilities for training in-patients, as well as for research work, (2) To provide Insulin free or at a nominal cost to poor and middle class patients, (3) To develop facilities for the education of doctors as well as the public in matters relating to diabetes, (4) To train nurses in special diabetic nursing, including calculation as well as preparation of diets (5) To cause researches to be undertaken specially to determine the etiology and best form of treatment with special regards to the local conditions and lastly (6) To work for the improvement of the lot of the diabetic.

The functions of the *Central Organization* would be as under — To control and co-ordinate the activities of the various affiliated associations in order to carry out an uniform policy, with modifica-

tions, if necessary, to suit the various areas, in matters of propaganda, diagnosis and treatment (2) To maintain a central research laboratory with a full-time staff to carry out some most intricate and labourious investigations (3) To assign, control and correlate the work of the various research centres and laboratories in order to avoid overlapping of work (4) To maintain a central bureau which would serve as clearing house for information and technical advice on all matters relating to diabetes (5) To run a central model clinic attached to the research laboratory

Planning of the Anti-Diabetic Campaign

To carry out such a programme is an herculean task requiring huge sums of money and a large army of workers. It would be therefore necessary to enlist and win the sympathy and support of the State, Politicians and Legislators, Rajahs and Nawabs, Municipalities, public health bodies like district and local boards and public welfare institutions, medical as well as nursing profession, and lastly charitable minded men and women of all castes and religions.

Any plan for combating diabetes is likely to be a failure until it is capable of being applied to conditions existing in cities and towns (where the disease is most prevalent) and effectually tackles the medical as well as social problems of individuals from various aspects. The various measures to be adopted may be grouped as under —

(1) Measures to provide diagnostic and treatment facilities which would be by way of (a) opening of special clinics and laboratories, (b) providing increased accommodation in city hospitals and opening of special diabetic hospitals or wards in existing hospitals, (c) encouraging private medical practitioners to diagnose and treat more patients

(2) Measures for carrying out researches with a view (1) to investigate into the etiology and (b) particularly to find out a standard treatment capable of being applied safely and easily and to a larger number of patients (3) Measures to arouse public opinion and to carry out educational propaganda work

I DIAGNOSTIC AND TREATMENT FACILITIES

Free Clinics and Laboratories

It has been rightly said that measures which fail to provide diagnostic and treatment facilities on a wide scale—by way of blood-sugar and urine-sugar examinations and free or cheap supply of Insulin to all whether rich or poor, and to guide people in matters of diet and personal hygiene are bound to prove more or less a failure. All these facilities are possible and can be provided, through the agencies of specially organized clinics. In a city like Bombay, a number of clinics could be started at convenient places, preferably one in each ward. For this purpose, the existing municipal and public dispensaries may be utilized, but a special hour may be fixed when

no other patients except those suffering from diabetes would be seen. These clinics should be able to diagnose and provide treatment at nominal or no charge especially to poor and unemployed patients. Nobody would deny that the conduct of these clinics must be maintained at a high standard and should be under the charge of persons who besides being good clinicians have received special training in diabetic pathology and laboratory methods as well as in principles of dietetics. There should be also an adequate personnel for the follow-up of cases.

These clinics need be regarded as clearing field—hospitals where patients suffering from different grades of severity of diabetes may be sorted out. Those whose condition is serious may be sent to hospitals for treatment as in-patients, whilst ambulatory type of patients may either be treated in the clinics or sent back to their own private practitioners, if the latter possessed sufficient means and knowledge to carry out the treatment. The success in the fight will much depend upon the efficiency with which these clinics are run.

Laboratories should be attached to the various clinics or arrangement may be made with municipal and hospital laboratories for carrying out on request, urine and specially blood sugar estimations. Examinations may be done either free or at nominal fees.

Hospitals

Wherever and whenever possible, hospitals specially meant for treatment of diabetes should be erected. But until such time, provision should be made in existing hospitals for a sufficient number of beds (some of them may be endowed) for receiving increasing numbers of diabetic patients, preferably in a reserved ward. The latter should be put under the charge of a specialist with a staff of well-trained nurses. The physician should be able to receive the co-operation of (a) a dietitian who should be able to compute and prepare diet to suit the needs of the different patients, (b) a chiropractist to supervise the care of the skin and to advise on footwear in order to prevent gangrene, (c) a radiologist, to make annual examination of the chest, to detect early signs of tuberculosis of the lungs to which diabetics are very prone and (d) a pathologist skilled in the technique of urine analysis and blood-sugar estimations.

In hospitals attached to teaching colleges or institutions, arrangements should be made for the training of under—and post-graduates in the specialized methods of diagnosis and treatment of diabetes. Nurses should also receive instructions in methods of special diabetic nursing together with in preparing recipes and cooking of diabetic foods. Further there should be a close co-operation between the hospital staff and the research department and one or two beds may be set apart for research purposes.

Dietary Department

It is highly desirable that every hospital should have a dietary department, placed under the charge of a person specially trained

in dietetics with a good knowledge of human physiology. The chief duties of the dietitian would be (1) to carry out the prescriptions of the physicians written in terms of grammes of protein, fat and carbohydrate and (2) to teach patients attending the out-patient department to carry out the instructions given as regards diet at home. The dietitian should be also a good cook, as to render the prescription into varied and attractive meals and to advise patients how to cook the prescribed diet themselves. He should be able to advise on matters relating to diet and to plan out research diets. In hospitals attached to medical colleges, the dietitian should be expected to impart theoretical as well as practical knowledge to the under-graduates in principles of dietetics.

Convalescent Homes and Holiday Camps

On account of comparatively restricted accommodation in hospitals and a long waiting list, patients are often discharged before they have completely recovered. Many of these patients have very often to come long distances for treatment at the out-patient departments, and because of unsatisfactory conditions at home, they suffer much inconvenience and hardship. To obviate this difficulty special convalescent homes should be established at suitable places with trained nursing staff and in charge of doctors who are well acquainted with the disease and able to carry out urine and blood tests. In the convalescent homes, effects of diet should be carefully observed and adjusted. Diabetic patients should also be treated for other complications except tuberculosis. Injection treatment of Insulin and other measures such as exercise, bath and massage should be carried out with a view to improve their sugar tolerance. It is here that the diabetic may be made to learn how to live his future life in comfort.

It would be a great advance if short holiday camps are opened by some enterprising diabetics or by welfare societies for diabetics at convenient hill stations or seaside resorts, where mentally worried or bodily fatigued diabetics may go to on short holidays. Many of the diabetics would not grudge to pay for their stay at such camps.

Diabetic Restaurant and Hotels

By the way it may suggested that in big cities where there exists a large number of diabetics, arrangement should be made with certain restaurants and hotels at which one can obtain diabetic food preparations at comparatively cheap rates.

Private Practitioners

Private medical practitioners specially those engaged in general practice occupy an important place in the plan of an anti-diabetic fight. They are usually compared to shock troopers engaged in a battle, because it is on them that falls the chief burden of making diagnosis and treating a large majority of cases in the early stages.

of the disease. It is they to whom a large section of the community flock for treating all kinds of maladies to which human flesh is heir. There are for instance in Bombay more than 2,000 doctors (excluding valdyas, hakims, quacks and charltans) and they all combined see or have the opportunity to see or detect more diabetic patients than all the hospitals, public dispensaries and the specialists put together. If they are given facilities for making urine and blood examinations they would be able to discover and treat many times more cases perhaps to the enormous benefit of the human kind.

It should be one of the chief aims of the diabetic associations or public health bodies to encourage private practitioners in discovering and treating diabetic patients in larger numbers in one or more of the following ways:

(i) *Free urine and blood examinations* —Arrangements should be made with municipal as well as government laboratories or those attached to large hospitals for carrying out urine and specially blood examinations at moderate or no fees especially in the case of very poor patients on recommendation of the private practitioner. The reports of urine and blood sugar examinations of course should be sent direct to the doctors, with necessary remarks on the findings.

(ii) *Free consultations* —Arrangements should also be made with consultants or experts to examine free or at reduced fees either in special clinics or at their rooms by private arrangement, whenever a private practitioner makes a request. The patient should be directed back to his own doctor, and findings of the case and necessary instructions for the treatment sent directly to the doctor.

(iii) *Free supply of Insulin* —In order to enable private practitioners to treat a larger number of diabetic patients especially those who cannot pay the full regular fee of the doctor, provision should be made for the free supply of Insulin from time to time and in quantity sufficient to last for about one to two months.

By these measures, private practitioners will be able to give care and treatment to very large number of patients. The general practitioner, on the other hand in order to render an useful service, will be required to know many things about diabetes. He should be able to do tests for sugar and acetone bodies in the urine, and should be able to diagnose early symptoms of acidosis, and other complications, and have also received training in dietetics.

Follow up of Cases

The services of specially selected and trained nurses should be made available for visiting the homes of the diabetics and giving necessary instructions in matters of diet and personal hygiene. Visits by nurses and medical inspectors are important specially to follow up lapsed cases and should be made when requested by a doctor. An efficient system of following up should be developed as prolonged treatment is the only weapon against warding off an otherwise early death.

II RESEARCHES

Though we have now, at our disposal highly efficient Insulin and its new derivative, we are not justified in regarding diabetic problems to be completely solved. There are many things which require to be cleared up and further researches are absolute necessity. The first and most important thing to be done is to find out a substitute for Insulin which would admit of oral administration and do away with injections. When this is done, it would be a great event in the history of diabetes, perhaps next to the discovery of Banting. We do not know yet what the precise influence of heredity is, what it is that determines the onset of disease in some members of the family while others escape, and the methods by which to detect children showing a hereditary tendency for developing the disease. We are equally ignorant of the precise influence of the nervous system on pancreas and of the part played by infections in lowering the sugar tolerance in diabetic patients who require the use of Insulin in much larger doses than otherwise. In recent times, the pancreatic theory of diabetes is itself challenged and several endocrine glands have been blamed as the root cause of diabetes. All such matters require to be worked up and finally settled before exact methods of treatment and prevention can be formulated. Hence much of our attention at present should be directed to the furtherance of research and study into the basic problems of diabetes. Researches do not only mean the services of trained doctors but also money and organization. The government and the public must be persuaded and prevailed upon to donate enough money for research purposes. Medical colleges and universities shall have to accord a rightful place to research in diabetes by generously endowing it, and by affording both laboratory and clinical facilities to research workers.

Conferences and meetings should be arranged where doctors in charge of diabetic clinics and others interested in diabetes may meet together, compare their work and exchange views on the subject with each other. The general practitioner must be made to take greater interest and kept informed of the advances made in the knowledge of diabetes from time to time.

Diabetic patients even themselves can help a good deal in promoting research work by providing valuable materials for research workers. By carefully following up their family history, they can give valuable help in determining the influence of heredity on the disease. They should have their children examined at regular intervals so as to detect any tendency to develop the disease as early as possible. Lastly by following accurately the instructions of the doctors and carefully noting the effects of particular experimental diet and other treatment, they can render very useful help in determining methods for improving the treatment. In fact, one of the main aims of future investigations is to arrive at a standardized treat-

ment including diet which could be applied to a large majority of diabetic patients and be utilized on a nation wide scale

Diabetes a Reportable Disease

Our knowledge of the incidence of diabetes is very imperfect and diabetic deaths do not throw much light upon it To perfect our knowledge it would be necessary to make diabetes though not a communicable disease, a reportable disease All reports should however be strictly confidential and should only be made use of for statistical purposes This source of information will be found more useful in judging the progress of our fight against diabetes

Special Case Recording

In order to determine the relative importance of the several etiological factors and to evaluate the importance of different methods of treatment with a view to improve and formulate a standard method of treatment which may be applicable to a larger number of patients, it is necessary to adopt an efficient method of recording the personal and family history, symptoms, and various etiological factors This is virtually impossible unless some set form is used for recording the facts The specimen copy of the form which is used at the New York Postgraduate Hospital is given below

SPECIMEN CASE FORM

Name		Dispensary No
Address	Age	Date
	Sex	
Race	Birth place	Religion
Occupation		

Diabetes Mellitus.

Diagnosis

History taken by —

I Heridity

- a Diabetes Mellitus
- b Goitre
- c Obesity
- Tuberculosis

Father
Brothers

Mother
Sisters

- e Gout
- f Heart disease
- g Nephritis
- h Apoplexy

- II Personal
- a Alcohol
 - b Tobacco
 - c Tea Coffee
 - d Dietary habits
 - e Genital
- III Past history
- IV Sugar first discovered
- V Onset, date symptoms
- VI Possible preceeding symptoms
- VII Why was urine examined for sugar?
- VIII Possible etiology (describe and give duration and date of each symptom)
- a Obesity
 - b Trauma
 - c Pancreas, abdominal pain, character of stools etc
 - d Nervous
 - e Thyroid exophthalmos, Thyroid enlargement Vomiting Nervousness Tremor, palpitation, Diarrhoea
 - f Hypophysis, acromegaly Gigantism.
 - g Kidney, Headache Visual disturbances, Dyspnoea, Oedema Albuminuria
 - h Liver, skin pigment
 - i Unknown.
- IX Previous treatment and results
- X Symptoms since onset of disease (date of each and relation to any treatment)
- a Wt lbs to-day
 - b lbs highest loss from highest wt
 - b Loss of strength
 - c Polyuria
 - d Nocturia
 - e Polydipsia
 - f Polyphagia
 - g skin, pruitus Furunculosis other conditions
 - h Pains
 - j Cramps
 - k Mouth
 - l Bowels
-
- XI Other symptoms
- a Digestive
 - b Circulatory
 - c Renal
 - d Respiratory
 - e Nervous
-
- XII Present complaint
-

Social Amenities and Employment Bureau

The social side of the diabetic question is of tremendous importance. Diabetics are not taken up in certain services and are often found unsuitable for certain kinds of work on account of their physical debility. They thus tend to swell the numbers of unemployed persons. They cannot freely participate in many forms of amusements and active games like hockey, cricket and foot-ball. All this tends to produce in them depressed states of mind which should however be prevented by all possible means. It would be a great boon to open an employment bureau with a view to find out suitable jobs for diabetics. The clerical occupations are particularly suitable because they require very little expenditure of physical energy and do not expose diabetics to undue danger. On the other

hand certain occupations, specially those involving heavy manual labour with irregular hours of meals or great responsibility as in motor driving are not suitable for diabetic patients

Social amusements may be provided to poor diabetics by way of arranging free cinema shows or excursions to nearby woody or sea side resorts or holding camps in summer days where diabetics could meet together under the supervision of trained doctors and dietitians. A good library containing a large number of popular books on Health and Hygiene and a good gymnasium where graded exercises can be given to diabetic patients are extremely desirable

III EDUCATIONAL PROPAGANDA

Wide spread education of the public in matters relating to diabetes should be a big forward step towards eradicating the disease from the community. The purpose of educational work must be to make people to take more interest in diabetes rather than to frighten them by magnifying its terrors. The public should know what diabetes is, how it is caused, how the disease may easily be recognized, what the relative advantages of frequent urine examinations are, what the dangers of neglecting or not taking adequate prophylactic treatment are, and many other like things. In fact the public must be so much educated that they should atleast be able to recognize the early symptoms of diabetes and seek medical advice before the disease is far advanced.

In this kind of valuable work the general medical practitioners are obviously the most appropriate persons, because it is to them that the great many people turn for information and future guidance, and secondly, professional knowledge and opinion greatly influence this kind of public health instruction. Besides, holding lectures and classes the educational work should include cinema demonstrations, health exhibits, distribution of literature in different local languages and exhibition of posters. The chief aim of education should be to stimulate interest in diabetes and then to instruct

Quack & Secret Remedies

A minor part of the educational work should be devoted to warning the people against the futility of resorting to secret and proprietary remedies advertised in the lay press and intended to be used in self treatment of the disease. Warning should also be given against the activity of a large army of quacks and charlatans who claim to be able to cure diabetes easily, quickly and by secret methods, instead, the full value of dieting and exercise should be carefully impressed on the minds of the public.

In order to obtain appreciably good results the educational work must be continuous and long sustained, and should be in the hands of well organised societies or official agencies.

The collective or public health measures though calculated to relieve much distress and suffering are seldom likely to succeed

unless the diabetic or could be diabetic willingly and faithfully co-operates with his doctor and is individually treated and cared for

It has been already observed that it is very difficult to obtain absolute prevention by any known methods except only (1) by preventing marriages between persons belonging to family of known or unknown diabetics and (2) by preventing or treating obesity in its early stages, in case we accept heredity and obesity as the chief forces or factors concerned in the development of susceptibility for diabetes

Prompt and Early Treatment

It has been made abundantly clear that diabetes when early recognized and promptly treated usually runs a smooth and mild course and is easy to control, and that under continued treatment not only are the serious complications indefinitely warded off, but often times there is marked and permanent improvement in the sugar tolerance of patients which renders the use of Insulin unnecessary after some time. In fact the life of an adequately treated diabetic hardly differs materially from that of a non-diabetic person

Fortunately, it has been found that in the case of diabetes there are no marked fundamental differences between the curative and preventive measures which in a sense may be regarded as closely blended together. In fact there should be no fundamental distinction between the curative and preventive medicine because the aim of all medicines is after all always the same, viz, "To prevent bad from going to the worse"

Critical Notes and Abstracts

THE HYPERACTIVE CARDIOINHIBITORY CAROTID SINUS REFLEX

Sigler, L.H Arch Int Med, 67 177 (1941)

There is no doubt that the normal carotid sinus mechanism represents one of the many compensatory mechanisms of the body concerned in the maintenance of a normal circulation. Stimulation of the carotid sinus occurs as a rule with alterations in the intracarotid blood pressure. If the response to such a stimulus is excessive as shown by an extreme degree of fall of blood pressure, cardio-inhibition and cerebral symptoms, then we have what is called a "hyperactive cardioinhibitory carotid sinus reflex."

Sigler, after investigating this reflex in a large series of cases (1,886 cases) comprising of 1,151 males and 735 females, has come to the following interesting conclusions (1) the reflex occurs with greater frequency and with greater violence in males than in females, (2) with increase in age, there is a corresponding increment in frequency and degree of the response, (3) the reflex occurs with the greatest frequency and with the highest degrees of response in coronary disease, it is roughly proportional to the severity of the coronary disease, (4) when the response is hyperactive in order diseases, it seldom attains the high degree of response of the coronary case.

Because of the above findings, Sigler suggests the use of this reflex as a diagnostic aid in cases of suspected coronary disease in persons of middle age. The hyperactive carotid sinus reflex is attributed to a lowering of resistance at the synapses in the (1) cardioinhibitory centre (2) intra and extra cardiac ganglionic cells and (3) myoneural junctions, as a result, the transmission of stimuli or impulses, afferent and efferent, occurs with ease and in an overwhelming manner.

A further study of the reflex may serve to unravel many mysteries connected with arrhythmias of the heart as well as with the phenomenon of "sudden death"

R J VAKIL

FACTORS AFFECTING THE TESTS OF KIDNEY FUNCTIONS

Raymond C Herrin, (Physio Rev Vol 21, No 4, Oct, 1941, pg 529) has discussed mainly the urea clearance test, and has reviewed the results obtained by a large number of workers. As a result of the review the author has arrived at the following conclusions

Urea clearance is not affected directly by interference with the nerve fibres to the kidneys, either in experimental animals or in

human beings subjected to therapeutic Splanchnectomy The amount of urine may vary only as the blood pressure is changed by this procedure

The actual administration of urea before the test, with a view of raising the blood urea to its maximum value is advocated by many, giving more accurate and consistent values The rise in blood urea after urea administration does not alter the urea clearance In human beings the blood urea may change five times without lowering the clearance readings Fowweather from observations on normal human subjects found that previous administration of urea had the advantage of equalising the average normal values for urea clearance An abnormally low clearance is occasionally met with in normal fasting subjects The effect on patients with nephritis is different according to the extent of kidney damage The clearance is better after urea ingestion, in mild cases, but is poorer in acute cases Marked anaemia causes a distinct lowering of urea clearance and as the anaemia clears up the clearance returns towards normal This has been observed in pregnancy anaemia as well as in Pernicious anaemia,

The effect of diet is dependent upon the amount of urea-producing food stuffs This is marked in animals who show a distinct improvement in clearance with a high meat diet In human beings, because of comparatively smaller amount of protein ingestion, the improvement is less marked Cane sugar or alcohol in food has no effect on urea clearance

Vitamin A in food has a distinct effect on urea clearance, the clearance being poor if there is experimental avitaminosis

The amount of Sodium Chloride in food, has no appreciable effect on the urea clearance, unless a salt free diet is maintained for a very long time If there is a temporary deficiency of salt in the diet, the reserve Na of the body is mobilised and the NaCl concentration is maintained for a long time It is only after a marked depletion of the Na reserve of the body, that clearance shows a moderate increase

Muscular activity increases the clearance value, probably by increase in the excretion of urea, resulting from muscular activity

Pregnancy in normal women had no influence on the clearance In toxemias urea clearance is of considerable value in differentiating between pre-eclamptic state, nephritis and essential hypertension A high clearance value before delivery excludes chronic nephritis or essential hypertension A low value is not of definite help in the differential diagnosis If the clearance rises again after delivery it is indicative of pregnancy toxemia.

Hormones do not significantly affect Urea clearance Diuretic drugs like caffeine, or salyrgan do not affect the urea clearance In

essential hypertension the lowering of the BP by thiocyanate did not change the urea clearance

During fevers the urea clearance actually rises to higher than normal values and is slightly depressed during convalescence

Age In children a correction for body surface area has to be applied. Then the results are similar to those in adults and are rather on the high side. In old persons the clearance diminishes, but the decline does not follow a straight line regression but forms an N loop. There is a primary decline from 49 to 58, then there is a stationary phase, then a rise in the clearance.

K MANOHAR

X-RAY DIAGNOSIS OF PULMONARY TUBERCULOSIS

The X-ray shadows of pulmonary tuberculosis in its varying types and combination of types are so typical in their appearances and location that the wise pathologist at necropsy will use all the resources at his command before he disputes the diagnosis of the roentgenologist. With this introductory remark, Birkelo and Brosins present a series of cases in each of which a diagnosis of pulmonary tuberculosis had been made from the X-ray appearances and the clinical history, and in all of which cases the major illness subsequently proved to be non-tubercular. The conditions simulating tuberculosis sufficiently to produce diagnostic errors were—broncho-pneumonia, pulmonary abscess, bronchiectasis, pulmonary cystic disease, primary cancer of the lungs, metastatic cancer, silicosis, pulmonary moniliasis, actinomycosis, blastomycosis, and syphilis of the lung. Coronary disease and chronic valvular heart diseases with congestive cardiac failure also produce infiltration and fibrosis which simulate pulmonary tuberculosis. (Whooping cough and multiple areas of collapse in spasmodic states produce a picture which is very like one produced by military tuberculosis.)

“Our mistakes, appreciated and corrected, teach us more than our successes, and each difficult case, finally solved, leads to a better understanding of other diagnostic problems. The more we can share our experiences the better will be our mutual understanding, the more tolerant we become of the mistakes of others, and the more efficient we become as individuals.”

SUTHERLAND—Am J Med Sc Nov '41

PRIMARY TUBERCULOSIS

Sudden onset of a tuberculous infection is much more common than is realized. Its frequency is only realized after the routine use of roentgenoscopy in all acute cases.

Sweany has studied the primary tuberculosis in children and classified the X-ray appearance in the following six groups

Group i—Small foci communicating with the bronchi, frequently not visible until the disease has well advanced with massive involvement

Group ii—an ephemeral type of lesion that usually left no calcified tissue at all, lymph nodes involved, calcified foci in a few persons—clinically “tuberculin-positive X-ray negative” cases

Group iii—commonest type Lesions of this group leave behind only one calcified focus in the parenchyma—“Ghon’s tubercle” 85 per cent of cases of primary tuberculosis are of this type The lesion shows a single area of infiltration with definite central caseation, cloudy infiltrate, with poorly defined borders, which gradually clears from the nebulous mass to a more discrete shadow with a sharper border The size decreases rapidly in the first year, later the decrease in the diameter is about 10 per cent per annum for several years The decrease is due to laying down of the fibrous tissue each year for 6 to 8 years and later by a process of resorption from within The onset of primary tuberculosis in childhood is insidious and is attended with little more than an ephemeral initial fever which is frequently considered as “influenza” It is to be diagnosed from pneumonia The fever lasts rarely more than a week or 10 days and may last only for a few days In the majority of cases primary tuberculosis is asymptomatic within 2 weeks after its appearance of the allergic phase Marked symptoms suggest beginning ulceration or mixed infection

Group iv—in which large infiltrations had been resorbed and had left behind various “shrapnel-like” areas of calcification A whole lobe may be affected, and a large focus may clear leaving behind a large number of calcified foci

Group v—cases in ulceration or overflowing of the lesion led to an exacerbation of the disease A primary focus may ulcerate and set up disease One lesion out of a 100, ulcerating like this and opening in a bronchus will explain much of the adult type of tuberculosis

Group vi—is concerned with the haematogenous spread of bacilli through the lymphatics or blood stream after primary infection The X-ray picture is that of miliary calcification widely distributed throughout both pulmonary fields

The clinical significance of the primary tubercle was summed up by Sweany as follows “The majority of lesions do not spread at all, that is, they heal A relatively small number progresses, but because so many of these come to the attention of physicians, they seem to be relatively more numerous than they actually are A common type is the one in which several foci progress simultaneously, as in silicosis

and in non-immune races of people. Occasionally only one tubercle of the primary complex progresses and becomes obliterated, the remainder of the tubercles are left as healed "Ghon foci" and there is no evidence of the cause of spread of the disease. The reason for these progressive lesions is still one of the unsolved problems of tuberculosis. Such tubercles might appear to be recent fibrocaseous formations, yet they may have been enlarging over a period of years, it was possible to observe this in a study of serial roentgenograms. The capsule was apparently inadequate to hold the organisms within the centre of the focus. The reason for the breakdown of the defence mechanism varied, this might be due to partial exhaustion of the defence mechanism which allowed continual escape of the organism through the thin-walled capsule. It might be due to an increase in virulence of a particular colony of bacilli. A factor in the creation of the roentgenographic image of some of the lesions might be the spread of toxins causing a stimulation of new fibrous tissue outside the bronchioles, these structures become obliterated and enmeshed in capsule, as the spread continues into neighbouring alveoli and fibrosis. A few organisms might follow down the bronchioles or lymph tracts, some might get into the capillaries and travel to other parts of the lung or of the body. Because of the comparatively small number of these organisms, most of them are destroyed. Not until the tubercle encroaches on a larger bronchus or blood-vessel is there real danger of sufficient spread to cause clinically significant disease."

C G SUTHERLAND—*Am J Med Sc* Nov 1941

FURTHER EXPERIENCES WITH THIOCYANATES

Barker, Lindberg and Wald (*JAMA* 8th Nov 1941 pg 1591) have treated 246 patients during the past 10 years. Thiocyanates were employed when the other usual clinical measures had failed. The dosage was controlled by determination of cyanate concentration in the blood. A concentration of from 8 to 12 mgm per 100 cc was found to give the best sustained symptomatic relief and improvement in blood pressure without endangering the welfare of the patient. The studies show that there may be great individual variations in the rate of excretion of the drug and that the same patient shows variations of concentration depending on the fluid balance varying with season, fluid intake and with physical activity. In general the treatment is begun with 5 grains of pot thiocyanate daily, and the blood cyanate concentration is determined at weekly intervals for 4-6 weeks. Throughout the whole course the dosage may be constantly varied, depending on the patients' symptoms, blood pressure and blood level concentration. Symptoms of fatigue, somnolence and mental retardation often met during the first 4 to 6 weeks of treatment are not as a rule indications for discontinuance, although the dosage may be moderated. The systolic blood pressure may drop during the first 2-4

weeks while the diastolic blood pressure may not show a persistent reduction for 3-4 months. An occasional patient may show no response for 3 or 4 months. Excellent results may be obtained in all age groups, but caution should be exercised in patients with poor renal function. Once the symptoms, blood pressure, dosage and blood cyanate level have been satisfactorily correlated, the patient should return for check ups at intervals of 1-3 months.

Little or no benefit has been obtained in severe hypertension with fixed blood pressure in which blood counts are below 4.5 million per cubic millimetre, with a progressing anaemia and a rising sedimentation rate. In any case of hypertension with signs of cardiac decompensation, an attempt should be made first to improve the cardiac function before cyanate therapy. Of the 246 patients treated 47.5 per cent have shown persistent improvement in the symptoms, clinical status and blood pressure for over a 2 to 11 year control period. In addition 19.5 per cent have shown significant reduction in blood pressure without any definite changes in their clinical status, another 9 per cent have shown symptomatic improvement without alteration of blood pressure. Thus 76 per cent have received some benefit.

In some patients symptoms appeared to occur as the result of the reduction of blood pressure which disappeared when the blood pressure was allowed to rise to a certain level. In other patients symptoms of extreme depression, word aphasia, slurring speech, unsteady gait and disorientation appeared when the blood cyanate concentration was above 20 mgm per 100 c.c. and disappeared when the drug was discontinued. It is not unusual, however, to see fatigue, secondary anaemia and a dry scaling skin appear after many months of continuous ingestion of cyanate. If the red cell count drops below 3.8-4 million, the drug is discontinued. The dermatitis may manifest itself in several ways. An occasional large thyroid develops or a myxoedematous facies with low basal metabolic rate but all these cases have shown recovery with 1-2 grains of thyroid daily within 2 weeks.

Severe cyanate poisoning in dogs (40 to 65 mgm per 100 c.c. blood concentration) shows no changes in any organ except damage to the liver and bone marrow, resembling benzene poisoning. The only additional changes in the dogs were reduced red cell counts, blood cholesterol and total serum protein findings which could be explained on the pathologic changes mentioned.

A. S. P.

THE HARMFUL EFFECTS OF MINERAL OIL (Liquid Paraffin) PURGATIVES

Moryan, (J.A.M.A. 18 Oct 1941, pg 1335) states that the wide use of liquid paraffin seems to be based on empirical considerations. Its chemistry is, to say the least, uncertain and its pharmacological

action, a matter of dispute. It is a laxative and usually induces soft and liquid stools. But its use as a laxative may be severely criticised on the grounds that (1) It interferes with the normal physiologic process of evacuation of the faeces. The rectum is not a reservoir, but functionally it is a short passage. Once faeces enter the rectum, they should be evacuated with the establishment of the defaecation reflex. With the use of liquid paraffin the competence of the rectosigmoid valve is destroyed and as a consequence the reservoir effect of the sigmoid and the descending and the transverse colon is lost. Continued leakage from above results in the rectum being kept partially full most of the time, while there is not sufficient to initiate the defaecation reflex, but there is enough faecal material present to cause symptoms of initiation. Complete evacuation of the rectum becomes impossible, and there is always a tenacious layer of a dirty mixture of oil and faeces covering the rectal mucosa. Patients with rectal disease frequently take liquid paraffin but it often serves to aggravate the local lesions by making a faecal reservoir of the rectum.

(2) Because of its preferential solubility, it interferes seriously with the utilisation of carotene and to a lesser extent with vitamin A concentrate as well as with the fat-soluble D.

(3) It hastens the motility of the bowel contents in the small intestine and, as a consequence, digestion is incomplete. The reduction in the absorption time may help to explain the loss of weight and strength which so often occurs in the patients habitually using it. There is clinical evidence that persons who have taken it over a long period of time suffer from "indigestion." This is perhaps due in large measure to interference with absorption from the small intestine.

(4) Evidence is accumulating that liquid paraffin may be absorbed producing pathologic changes in the liver and other abdominal viscera, producing a syndrome which may be called "mineral oil poisoning." The most frequent symptoms are anorexia, indigestion, flatulence, fatigue, nervousness, dyschesia and anal leakage. Many suffer weight loss. Treatment is the discontinuance of the oil along with supportive measures to overcome the weakness which accompanies the symptom complex. The mechanism of its laxative action is disputed. Some contend that it acts mechanically by softening the faeces, others hold that it undergoes emulsification and still others assert that it speeds up peristalsis by its irritative action on the mucous membrane. There is also the concept that it is an intestinal lubricant. The contents of the intestine, except for about the terminal three feet, are liquid and this fluid needs no lubricant.

Thus the internal administration of liquid paraffin either alone or in combination with other substances may be attended by decided disadvantages

ACTION OF BISMUTH CARBONATE IN GASTRIC DISEASE

Alstead (*Lancet*, 11th Oct, 1941, 420) discusses the use of bismuth carbonate and bismuth subnitrate as gastric antacids and sedatives. Bismuth subnitrate has now fallen into disrepute, the carbonate, on the other hand, is widely used in the treatment of gastroduodenal disease, especially in cases of peptic ulcer and gastritis. Alstead has investigated the value of bismuth carbonate in relieving the pain of gastrointestinal disease and the investigations provide no evidence in favour of the view that this salt in therapeutic doses protects the gastric mucosa. After administration by mouth, the salt collects in the most dependent part of the stomach and there is a tendency for it to adhere to the mucous membrane in a relatively small area in the prepyloric region, but the ulcer bearing area of the stomach is rarely affected.

Bismuth carbonate may exert an astringent action on the empty stomach, but the investigations show that even under favourable conditions this must be very slight, and in practice it must be rendered negligible by the combination of the minute amount of bismuth in solution with the muco-protein of the gastric juice. It is also an unsatisfactory antacid for clinical purposes. The antacid effect following therapeutic doses of bismuth carbonate is seen to be trivial or entirely absent. The findings support the view expressed by Hurst in 1929 "It seems very improbable that the small doses of bismuth (carb) given with sodium bicarbonate in the usual alkaline mixtures, powders and tablets can exert an action of any kind in the stomach. Its use should therefore be discharged, as it has a disadvantage of making the stools black so that the immediate recognition of slight melaena by the patient becomes impossible."

A S P⁻

TYPHUS FEVER

In connection with the appearance of two case reports suggesting Typhus fever in Bombay, I wrote to the Executive Health Officer, Bombay Municipality, inquiring about the cases of Typhus from Bombay reported to the Health Department. He kindly sent me the following answer:

"In all 11 cases of Typhus were reported in 1941 and 3 during the current year so far. 13 out of these were reported by the Combined Military Hospital, Colaba, and one by Col Bozman, Port Health Officer, Bombay, in an Italian prisoner of war sent out of Bombay directly from the ship.

"No definite information as to the exact vector was available in all these cases except that lice or ticks which infested the jungle near the camp were suspected.

These cases I am given to understand, were not the typical Typhus of Text-books but probably a variety of Rickettsiosis. They responded in some instances to the clinical and laboratory tests

8 Tuberculosis is an old and dangerous enemy. It lies in wait particularly for the young adult, whose services today and after the war must be of supreme value to the nation. Moreover, tuberculosis always increases in wartime, and measures must be taken now if the increase that we may expect in the future is to be stemmed. Our existing tuberculosis services can normally deal with cases of the disease which are sent to them. These services in this country have grown up almost entirely since the last war. They deal with those who have symptoms of disease or who feel ill. But a new advance in the detection and prevention of tuberculosis is now needed. This means finding cases in whom the disease has started but not yet caused the patient to feel ill. Often nothing may be necessary other than careful watching, in some, short treatment is required, but in all cases there is a better hope of eradicating the disease. X-rays used wisely by competent physicians constitute a very important advance.

9 In this country government proceeds by consent, and anything savouring of compulsory examination would be foreign to our traditions, and would fail at the first attempt. The National Association believes that public opinion can be educated to recognize the needs of the situation, and appeals to the workers, employers, doctors, and other responsible authorities to consider the facts of tuberculosis as an enemy of youth and a menace to our national health in wartime. A valuable weapon is in our hand, the increased use of x-rays among all sections of the community, whether they feel ill or not, particularly in the young adults.

10 More careful application will have to be given by the Government and local authorities to the provision of economic security for the tuberculous family, as part of a national scheme of social welfare and rehabilitation. This will have influence on the willingness of tuberculous persons to accept early treatment.

11 There is reason to believe that the x-ray manufacturers will shortly be ready to provide apparatus as soon as they receive orders.

(Brit M J Feb 28, 1942)

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Psychotria seed I engtreek,
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Original Contributions

SHOCK AND ITS TREATMENT

By

R N COOPER,

MS (LON), FRCS (ENG) FRCPS (BOM)

BOMBAY

It is usual to describe shock as either primary or secondary. *Primary Shock* is observed in those cases where injury is so severe as to be fatal in a short time. It is generally associated with severe hæmorrhage. In the absence of a severe hæmorrhage primary shock is of neurogenic origin. An individual suffering from primary shock may show a partial recovery and then lapse into secondary shock within a few hours. Recovery can be complete.

Secondary Shock takes a few hours to develop after the receipt of injury. The present discussion is mainly about secondary shock. In its early stage shock can be successfully combated. If, however, the condition is allowed to persist, a stage is reached when shock becomes irreversible and the end is fatal.

It is not possible to define shock. It may best be described as a condition of depressed vitality following trauma in which some of the manifestations are recognised clinically and others are only appreciated by laboratory findings.

From the clinical standpoint the earliest manifestations of secondary shock is a rising pulse rate and a falling blood pressure. A systolic pressure persistently below 100 mm and a diastolic below 65 mm in a wounded man is indicative of danger. With the fall in the arterial pressure there is a similar fall in the venous pressure. Unfortunately, there is no clinical way of demonstrating this low venous pressure. Other symptoms soon follow. Temperature drops and becomes subnormal. The skin becomes cold and clammy. The forehead in particular is bathed in perspiration. There is an early restlessness which changes later into mental apathy. Where there is associated hæmorrhage, restlessness continues. The sense of

note that in a case of shock all the capillaries of the body do not dilate simultaneously. In a traumatised limb the capillaries of that limb are first affected and Blalock and his co-workers have shown that the weight of the traumatised limb is considerably increased. The release of a tourniquet from an injured limb permits this dilatation to come into operation. When the tourniquet is released, blood as it re-enters the limb finds its way into the dilated capillaries and is thus trapped and removed from active circulation. This produces a diminution of the volume of blood, a lowering of blood pressure and precipitation of shock.

The sudden appearance of shock after the release of tourniquet as observed in wounded soldiers during the last war, was ascribed to a sudden absorption of a large dose of histamin like substances liberated from the traumatised limb. Probably both the factors are at work.

As shock advances it is easy to conceive that the dilatation of capillaries will extend into other body areas and diminution of blood will be further accentuated.

This trapping of the blood in the capillaries will account for the diminution of blood and the fall of blood pressure. However it will not explain the *concentration of blood*. A drop of blood removed from a patient in shock shows a marked increase of red blood and white blood cells. This phenomenon can be explained by the fact that in shock the permeability of capillaries is increased so that the fluid part of blood—plasma—escapes from the capillaries into the tissues. As the plasma thus leaves the blood it tends to make the blood more concentrated. Again here too capillary permeability is increased in certain areas only and the increased concentration of blood may be compensated to certain extent by the passage of fluid from the tissues into the blood in these areas where capillaries are still normal. This compensatory mechanism is responsible for recovery of cases of shock under adequate treatment. The concentration of blood increases its viscosity and offers additional impediment to efficient circulation.

The blood pressure as it falls may fall below the critical level which is approximately 80 mm Hg. Below this level flow of blood is so poor that there is a definite interference with the delivery of oxygen to the tissue. Thus there is tissue asphyxiation. All tissues do not suffer equally as the result of asphyxiation. One further vicious effect of this asphyxiation on the capillaries is to cause their dilatation and also alteration of permeability. Recent experiments seem to show that the cortical hormone of the Adrenal gland may have a direct influence on the permeability of the capillaries. An exhaustion of the adrenal cortex causes increased permeability. Hence arises the importance of giving this hormone in the early stages of shock particularly arising from toxic factors, as in extensive burns. The tissue asphyxia affects the vaso-motor centre so that it loses its capacity to maintain the tone of the blood vessels. Once

this state is reached all remedial measures are futile. It may definitely be stated that systolic pressure of 80 mm or less if not raised permanently within four hours generally ends in death.

In the early stages of shock some differences are to be noted in the pathology of shock depending on the ætiological factor.

The Neurogenic factor plays an important part in primary shock. A severe wound or even a trivial injury in a highly strung individual will produce a reflex relaxation of blood vessels with a sudden drop of blood pressure. This diminution of pressure causes a dilatation of the capillaries with the locking up of blood in the capillary bed and a resulting diminution of blood volume. If the blood pressure falls below the critical level there is inefficient delivery of oxygen to the tissues, with resulting tissue asphyxia. This asphyxia produces further dilatation of capillaries and a damage to their endothelial cells.

Because of the damage to the capillaries the endothelial cells become more permeable. The increased permeability allows plasma to escape into the tissue spaces and the blood becomes concentrated. Within limits these changes are reversible. However, once the different vicious circles become fully operative, shock becomes irreversible. Thus one finds that some cases of neurogenic shock do recover and often promptly, under adequate early treatment such as relief of pain and blood transfusion. In cases of shock of nervous origin, anæsthesia, by cutting off the painful stimuli and by subduing the psychic factor, often brings about an actual rise of blood pressure, and an amelioration of the symptoms of shock. The value of morphine is thus explained.

Hæmorrhagic factor A large hæmorrhage is a potent factor in introducing shock. The diminution in the volume of blood and the low blood pressure induced can initiate shock. However in the beginning a certain amount of compensation occurs. The diminution in blood volume is quickly restored by the passage of fluids from the tissue spaces into circulation. The lowering of blood pressure is kept under control by the maintenance of peripheral resistance by the increased action of the vasoconstrictor centre. If, however, the blood pressure remains persistently low there will be an inadequate supply of blood and oxygen to the vital centres. Asphyxia of the vaso-motor centre will set the stage for irreversible shock by a dilatation of the capillaries and an alteration of their permeability. Thus in the early stages, shock from hæmorrhage is most readily treated by restoring the fluid lost. Intravenous injection of any fluid in a sufficiently large quantity quickly restores the arterial pressure. It need not be emphasised that blood transfusion takes the pride of place among the various therapeutic measures. To be effective such transfusions must be done early, before the vaso-motor centre loses its capacity to maintain tone.

Toxaemic factor is most commonly seen in all cases of delayed shock resulting from trauma or infection. Histamin-like products liberated as the result of trauma to tissues or bacterial products evolved as the result of infection seem to have an identical influence in bringing about delayed shock. The absorption of these toxic products in blood produces a dilatation of capillaries and an increased permeability of the capillary walls. A carefully planned out early treatment of open wounds which aims at the complete excision of all non-viable tissues and the early control of infection by chemo-therapy will do much to eliminate these factors.

The treatment of shock is best considered from two points of view. Some of the measures have both a preventive and a curative value. Other remedial measures are essentially employed when the condition of shock is established.

Preventive measures are directed against four cardinal factors which precipitate shock, namely, (a) cold, (b) pain, (c) hæmorrhage and dehydration, (d) toxæmia.

(a) The application of heat in one form or another makes a striking change in the clinical condition of a wounded man suffering from shock. Army manuals require that a wounded soldier should be so wrapped up as to have four layers of blanket encircling him. In an emergency, sheets of newspaper intervened between two layers of blankets will make up for a shortage of blankets. Other methods of applying heat suggest themselves. Hot-water bags suitably filled with hot water and encased in flannel covers are routinely used in hospitals. In an emergency any glass bottle may be filled with hot water and wrapped up in a towel or sheets of a newspaper. Hot water may often be obtained from the radiator of a car. Tiles, bricks, sand or pieces of stone may be heated over a fire and then wrapped up in paper or cloth and used as good substitutes for a hot water bottle. Such heated articles should never come into direct contact with the skin of the patient or else severe burns will result. Cold wet clothes conduct away body heat and should be removed.

Another practical way of supplying heat is to give the patient hot sweet drinks such as tea or coffee. A patient in shock suffers from excessive thirst and he gratefully appreciates such a drink. In the later stages of shock vomiting sets in and then such drinks have no value. Never give a hot drink when a perforative lesion of the gastro-intestinal tract is suspected.

(b) Pain aggravates shock. Shock in cases of fractures is prevented by adequate splinting and immobilization of the fractured bones. The proper application of a Thomas's splint at the site of the accident should be taught to every A R P worker.

Morphia should be administered freely unless contradicted. $\frac{1}{4}$ grain is sufficient to allay pain in most cases. The same dose may be repeated if necessary. It is not wise to go beyond half a grain.

(c) *Haemorrhage and dehydration* A.R.P. workers should imbibe fair quantities of fluid during their duty hours and should not get into a condition of dehydration.

Bleeding of a considerable magnitude is often the prime factor in inducing shock. Therefore, every attempt must be made to stop bleeding. It is very tempting to supply a tourniquet to an open wound of the extremities. Such a simple procedure may produce several mishaps. If a tourniquet is kept on for more than twenty minutes it will seriously interfere with the vitality of the limb and produce gangrene. Therefore, the tourniquet should be loosened at intervals of 15-20 minutes. It should be reapplied as soon as bleeding starts again. In transporting casualties it is essential to mark the exact time of the application of the tourniquet on a card attached to the patient so that the receiving officer may have this important information in his hand. A tourniquet is at best a temporary emergency measure. Whenever possible it is best to ligate the bleeding vessel or employ direct pressure over the bleeding point by a pad of gauze or lint held in place by a firm bandage or rubber band (Esmark's bandage).

If, however, the limb is so hopelessly mangled as not to be saved, it is a wise policy to apply a tourniquet and leave it on until an amputation is undertaken. Such an amputation must be performed proximal to the tourniquet.

Fluid lost by hæmorrhage or dehydration should be replaced promptly. The value of hot and sweet drinks is already emphasised. Early blood transfusion where a blood bank is available is a boon indeed. In absence of whole blood, a solution of dried plasma-protein in distilled water may be utilised. A properly prepared 6% gum-acacia solution in 0.9 per cent of sodium chloride is still an effective measure. If these measures are not available an intravenous injection of normal saline (0.9 per cent sodium chloride) is quite effective. These early transfusions counteract the reduced blood volume, which is such an important pathological feature, and help to interrupt the vicious circle at its start and thus combat shock.

(d) *Toxaemia* may be either the result of absorption of toxic material from damaged tissues or the products of infection. The onset of gas gangrene is often the starting point of shock. At this stage it is necessary to point out the importance of early and adequate treatment of wounds. A wash with a mild antiseptic, a dab of iodine and a suture of the wound as practised in the casualty departments of some of our hospitals is to be strongly deprecated.

Under an anæsthetic the wound and the surrounding skin require a thorough cleaning with plenty of soap and water and a scrubbing brush. The damaged structures are to be freely excised so as not to leave behind any non-viable tissue. A complete hæmostasis is essential. The wound may be dusted with a sulfanilamide preparation. Sulfathiazole is particularly recommended. The wound may now be closed if practicable. It is treatment along these lines that will reduce the incidence of subsequent infection.

Treatment of established shock. The various preventive measures already discussed should be continued. Further treatment has a direct bearing on the pathology of shock. The important features of the pathology of shock are

- (1) Reduced blood volume and hæmoconcentration
- (2) Diminished cardiac output resulting in low blood pressure
- (3) Reduced delivery of oxygen

Reduced Blood Volume. By the time shock is established, vomiting becomes so marked that exhibition of fluids by the mouth is useless. Hence other measures should be instituted to restore the blood volume. In the early stages of shock, particularly of hæmorrhagic origin, where the vaso-constrictor centre is hyperactive, the administration of any fluid intravenously, such as normal saline, will quickly restore the arterial pressure. However, if the arterial pressure remains at about 60 mm. of Hg even for an hour, the vaso-motor centre is so affected as to lose its hold and the peripheral constriction gives place to dilatation. When shock is established and the permeability of the capillaries is increased such transfusions are useless. The blood is diluted and volume is increased no doubt, but because of the altered permeability the salt solution passes out from the capillaries into the tissues and the good effects are lost and the tissues on the contrary get water-logged. Such an accumulation of fluids may result in œdema of the lungs. A fluid, therefore, which contains ions in solution will readily pass out. To be effective a fluid should be employed in which the molecules are much larger than in the case of ionic solutions. Such a fluid should contain colloids and not crystalloids. These considerations led Bayliss to advocate the use of gum acacia solution (6%) in normal saline during the last World War. To-day this solution is entirely replaced by either whole blood transfusion or liquid plasma transfusion or dried plasma redissolved in distilled water. The use of citrated blood by the indirect method is sufficiently elastic to be applicable to all cases. The establishment of a blood bank makes this procedure easily available.

However, there are dangers attached to blood transfusion if attention is not paid to details. The whole blood transfusion not only replaces the fluid lost but also supplies the solid elements, the erythrocytes and the white blood cells which have a high therapeutic

value When citrated blood is allowed to stand in a cool place the solid elements settle at the bottom The clear plasma can be pipetted off This liquid plasma can be used for all shock cases It contains all the colloids with some crystalloids There is obviously no need for matching of blood when plasma is employed, as the erythrocytes are already removed Liquid plasma cannot be preserved for long, so it is dried and the dried plasma is readily soluble in distilled water and is thus very useful

All intravenous injections should be given at body temperature The rate of flow for blood transfusion should be about 15 cc per minute As regards the amount of fluid to be injected, it is to be remembered that there is a distinct risk of the tissues becoming water-logged In shock the capillaries are dilated and peripheral resistance is low Introduction of fluid causes the veins to be filled, but the arterial pressure does not rise The venous pressure rises and further embarrasses the heart The patient is in the same state as one suffering from heart failure It is unfortunate that venous pressure readings are not taken A safe rule would be to introduce only such an amount of fluid as would not raise the venous pressure above the normal level In absence of such a reading the amount to be introduced will always be guided by a certain amount of guess-work

(2) *Diminution of Cardiac output and Low Blood Pressure* Raising the foot of the bed, in the hope of supplying sufficient blood to the vital centres, is of doubtful value In secondary shock the stagnant blood is not in the veins and a head-low posture may prove irksome to the patient In primary shock with hæmorrhage, a head-low posture may be of value

The use of vaso-constrictor drugs like adrenalin, or pituitrin is now discarded However, in shock of toxæmic origin extract of Adrenal cortex has found favour It is supposed to influence the permeability of the capillaries favourably It is best given intravenously along with any intravenous transfusion

(3) *Reduced Delivery of Oxygen* Employment of a 100 per cent oxygen through a suitable mask, (B L B mask), helps in supplying this vital gas to the oxygen starved tissues

Operations and Shock It is a sound rule to treat shock first and delay operations to a later stage when the patient is sufficiently recovered There is, however, one definite exception An open-sucking pneumothorax requires an immediate closure The closing of such a wound brings about a marked improvement in the condition of shock A relatively small hæmorrhage will turn the scales against a person already in shock Hence an operation for the arrest of any hæmorrhage is definitely indicated even in absence of a definite recovery Similarly, a rapidly spreading infection calls for urgent surgery even before recovery from shock is stabilised A guillotine type of an amputation is best suited for such a purpose

Anaesthesia and Shock The beneficial effect of anæsthesia in primary shock of nervous origin is already alluded to. However, the choice of an anæsthetic is of considerable importance. The safest anæsthetic to use is a mixture of Nitrous Oxide and oxygen in the proportion of three of the gas to one of oxygen. A lower concentration of the gas may advantageously be combined with local infiltration anæsthesia employing $\frac{1}{2}$ -1 per cent of Novocaine.

During an operation speed and gentleness of manipulations are essential. All precautions should be taken against further loss of any blood. Body heat must be maintained. Undue lifting and turning of the patient is to be avoided. Should the blood pressure drop during an operation, an immediate blood transfusion should be resorted to. In the after treatment, sleep must be secured, fluid balance maintained and dissipation of body heat prevented.

PERIPHERAL CIRCULATORY FAILURE

By

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Shock, primary or secondary, is very frequent in surgical practice, but a similar clinical state known as peripheral circulatory failure is also common in medical practice. It is frequently met with in a variety of conditions such as acute infections, like pneumonia, enteric fever, septicaemia, severe anaemias, acute coronary thrombosis, acute intestinal obstruction, diabetic ketosis, Addison's disease, pulmonary embolism, acute pancreatitis, cholera, dysenteries, severe vomiting and diarrhoea and many other conditions.

Cannon¹ has stated that definition is not a prime requisite in such a complex as shock. Yet a working definition is necessary to study the phenomenon. It is suggested that "Shock is a condition of peripheral circulatory failure brought on by a discrepancy between the volume of circulatory blood and the size of the vascular system and leads to deficient blood supply to the tissues of the body. This discrepancy may be due to a reduction of the blood volume, or to an increase in the capacity of the vascular system or to both" (Blalock)². Harkins³ has defined shock briefly as "progressive vaso-constrictive oligemic anoxia".

All physicians are familiar with the clinical picture of the fully developed condition.

The patient is weak and restless. He has an anxious expression. The skin is cold and clammy, and there is marked pallor. The pulse is weak, of poor volume, thready, rapid and rising. The blood pressure low and falling. The superficial veins are collapsed. The breathing is rapid, laboured and shallow. There may occur vomiting, thirst, oliguria and sometimes diarrhoea. The patient gradually sinks into coma and dies.

The changes in the pulse and the concentration of the erythrocytes are the earliest signs of peripheral failure. The coldness of extremities is due to a reduction in bloodflow. Circulation is diverted to more vital structures, such as the brain, the heart, the adrenals. Though the skin temperature is low, the internal temperature may not be depressed. "The Blood Pressure does not fall greatly until after rather marked changes in the circulation have occurred. The Blood Pressure is not a good guide to the condition of the circulation in incipient shock but it is the best available index to the state of affairs

in shock that is more fully developed" (Blalock)² "It is important to remember that not all declines of blood pressure are of the same significance. There is a vast difference between two patients, both with a blood pressure at the critical level, when one has cold extremities and the other has warm or only slightly cool extremities. The patient who has a low arterial pressure and cold extremities usually has arterial vasoconstriction secondary to a significant reduction in the blood volume. The prognosis is usually very grave unless a sustained elevation of the decreased blood volume can be brought about by appropriate therapy. On the other hand, the situation is not so grave when the person with a low blood pressure has no significant reduction in blood volume. Vasodilation, instead of vasoconstriction, is present, and the condition will usually clear up spontaneously or will respond to vasoconstrictor drugs" (Blalock)²

This picture of collapse or peripheral circulatory failure is modified by the pre-existing disease and though it is easy to recognise it in its late stages, there is no method of diagnosing it in its early or incipient stages, nor is it possible to measure its extent.

Circulatory failure met with in medical practice may be (1) central or cardiac, (2) peripheral, and (3) combined. The first known as *Central or Cogestive cardiac failure* is characterised by passive engorgement of the systemic vessels or by congestion of the pulmonary vessels. Engorgement of the neck and arm veins, enlargement of the liver, dyspnoea, orthopnoea, cyanosis, oliguria and basal rales are its manifestations. *The peripheral circulatory failure* is suggested by extreme weakness, pallor, anxiety, restlessness, sweating, shallow rapid breathing, empty collapsed veins, rapid rising feeble pulse rate, falling blood pressure, and low pulse pressure. Very often the differentiation between the two states is very difficult.

Presence or absence of venous engorgement and congestion of the pulmonary vessels, the position of the patient, and the type of dyspnoea are helpful signs. Very often the diagnosis is to be made from the presence of the associated symptoms and signs pointing towards some likely cause of either peripheral circulatory failure or of central cardiac failure. The differentiation is important because the management of the two conditions is different. Combined cardiac and peripheral failure may occur especially in acute severe infections, coronary thrombosis and in pulmonary embolism. The manifestations of the peripheral failure may predominate and mask the cardiac failure.

In all acute infections, peripheral circulatory failure is an ever present danger. In most severe infections except perhaps in acute rheumatic fever and diphtheria, the cause of death is peripheral circulatory failure and not central cardiac failure. The mechanism of peripheral failure occurring in pneumonia or typhoid fever is not understood. The underlying factor may be damage of the capillaries by the toxins, increased permeability of the capillaries, with diffusion

of plasma into the tissue spaces, and stagnation of blood in the dilated vessels. Anoxemia may be responsible for the capillary damage, apart from the toxæmia. The decrease in blood volume results in a diminished venous return to the heart. For a period, peripheral vaso-constriction may maintain the blood pressure temporarily, but it produces anoxemia and capillary damage with extravasation of plasma. This loss of fluid may be measured by estimating the amount of hæmoglobin in the circulating blood from time to time, but this hæmoconcentration is not always present. The damaged capillaries may liberate some toxins but the evidence in its favour is meagre. The adrenal cortex plays some part in maintaining the normal capillary permeability and electrolyte balance. Meakins⁴ suggests the following hypothesis: (1) Through a single severe or repeated injury or infection the protective power of adrenals is stimulated, and if this compensation is sufficient it maintains cellular permeability even in the presence of excessive histamine. (2) If not, it permits histamine or histamine-like substance released from macerated or otherwise damaged organs, or that present in the blood and normal tissues, so to affect the permeability of the capillaries and the cells of a certain organ (and this in man is, firstly, the intestinal tract and secondly, the lungs) that large amounts of plasma and cellular fluid migrate into the pericellular spaces leading not only to a reduction of blood volume and its increased concentration but also to what may be called a cellular dehydration which affects many tissues but particularly those mentioned above. There is also dilatation of the capillaries and venules with stasis and thus increased areas to be filled by a diminished blood volume, anoxia and all the other manifestations of shock. Many of these still further conspire to increase capillary permeability and so the vicious circle is established.

Considerable amount of experimental work is done since the last World War to understand the pathogenesis of shock or peripheral circulatory failure. Unfortunately there is no standard method of producing a given degree of peripheral circulatory failure and there is no standard animal in which experiments can be carried out. The individual variations in different animals are marked and the interpretation of experimental results and their application to human problems is very difficult.

A detailed discussion of the pathogenesis of peripheral circulatory failure is not possible here, only the chief noxious factors that cause traumatic shock may be enumerated here (Harkins)³.

Initiating Factors. Injury. Traumatic, operative, thermal or chemical. To explain how injury causes shock, there are three theories: (a) Toxaemia Theory, (b) Nervous Theory and (c) Local Fluid Loss Theory, the last of which appears to be in favour at the present.

Accompanying Factors. (1) Oligæmia, (2) Diminished blood flow, (3) Diminished cardiac output, (4) Decreased metabolism, (5) Tissue

anoxia, (6) Capillary congestion, (7) Acapnia and acidosis, (8) Decreased muscle tonus, (9) Decreased venous pressure, (10) Low blood pressure, (11) Vasoconstriction, (12) Hæmoconcentration

Perpetuating Factors (1) Anoxia, (2) Hyperpotassemia, (3) Adrenalin medullary overaction, (4) Adrenalin cortical insufficiency, (5) Toxins and tissue metabolites, (6) Nervous factors

Types of Peripheral Circulatory Failure Blalock² has attempted a classification of peripheral failure into (1) Pure (a haematogenic, b neurogenic, c vasogenic) types and (2) Mixed types. The characteristics of these different types are summarised in the following table —

TYPES OF PERIPHERAL CIRCULATORY FAILURE					
1 Pure types			2 Mixed types		
	a Haematogenic	b Neurogenic	c Vasogenic		
Synonyms	Secondary shock Wound shock Traumatic shock	Primary shock			
Mechanism	Decrease in blood volume Vasoconstriction Decrease in cardiac output Decline in B.P.	Vasodilatation (splanchnic)	Vasodilatation	Complicated Preexisting illness, dehydration, anoxemia, psychogenic depression, neurogenic depression, haemorrhage, sweating, anaesthesia, loss of plasma, pooling of blood	
Chief initiating factor	Local loss of blood or fluid	Loss of constrictor tone	Histamine acting directly on the vessels	Not possible to ascertain	
Examples	External haemorrhage, Internal haemorrhage, (pleura, pericardium, peritoneum) Burns, loss of plasma Trauma, loss of fluid and blood	Primary shock Trasection of the cervical cord Spinal anaesthesia	Trauma, Crush Acute infections	Surgical operations, Infections Toxaemia Peritonitis Diabetic acidosis	

Management of Peripheral Circulatory Failure

It will be seen from the above brief that the problem of peripheral circulatory failure is a complicated one and no single line of treatment can be suggested for all cases. Each patient should be given individualised treatment after making an attempt to decide if the circulatory failure is peripheral, cardiac or combined. In the latter, manifestations such as coldness of limbs, low arterial pressure, rapid pulse, dyspnoea, and restlessness should be critically analysed to determine if due to central or peripheral failure. Treatment which is suitable for congestive failure, e.g., venesection, digitalis, sitting position, etc., is absolutely contraindicated in peripheral failure, while the most specific treatment for the latter, the introduction of fluids to increase the blood volume, will aggravate the congestive failure. Unfortunately in most cases seen in medical practice it is not possible to assess the part played by either type of failure and in the absence of a clear conception of the mechanism involved the treatment is often empirical.

1. *Secure rest and quiet* by checking exhausting symptoms, such as pain, insomnia, cough, restlessness. Simple sedatives and hypnotics may suffice in most cases, but morphia may be necessary in

selected cases A warning however may be given against the excessive use of morphia in cases of sever depression or vasomotor paralysis

2 *Avoid dehydration* Diarrhoea or vomiting should be checked Purgatives should not be used The patient should be well covered with blankets and undue exposure should be avoided Fluids should be freely administered by mouth or if necessary per rectum Thirst may be allayed by pieces of cracked ice

3 *Position in bed* In severe shock Selbye⁵ (1940) advised inversion of the patient as a first aid measure The foot of the bed should be raised and in carrying the patient on a stretcher, the stretcher bearer at the foot should carry the handles of the stretcher on the shoulder, while the rear stretcher bearer suspends the head at full arm's length

4 *Warmth* Blankets and hot water bottles in moderation should suffice Excessive warmth with infra-red lamps may do harm The depression of the skin temperature is a physiological protective mechanism, directing the blood to the vital organs, such as the brain, the heart and the adrenals Intensive efforts to raise the skin temperature may harm the patient Mason and Blalock⁶ found that animals in shock as a result of hæmorrhage or trauma survive longer with a depressed than with a significantly elevated skin temperature They do not advise cold applications but speak against heating devices unless the blood volume is increased by transfusion with blood or plasma

5 *Oxygen inhalations* In circulatory failure, both cardiac and peripheral, oxygen inhalations are useful The use of oxygen has not produced encouraging results in experimental traumatic shock, but its use is always indicated in circulatory failure in pneumonia, abdominal distension and coronary or pulmonary lesions

6 *Drugs* A warning is given above about the excessive use of sedatives A warning may also be given about the excessive use of vasospastic drugs Too vigorous a symptomatic therapy may actually do harm However, Kabat and freedom⁷ (1941) have recently reported that the slow injection of epinephrine will increase survival 300 per cent in animals with experimental shock $\frac{1}{2}$ -1 cc of *Adrenalin Hydrochloride Solution* (1:1000) may be used in a litre of 5 per cent glucose-saline given subcutaneously or intravenously This may be repeated every eight hours $\frac{1}{2}$ -1 cc of *Posterior Pituitary Extract* or *Ephedrine Sulphate* gr $\frac{1}{3}$ -1 may be used with the same purpose Diffuse vasomotor stimulants, such as *Coramine-Ciba*, *Cardiazol*, or *nicamide* may be used every three or four hours *Caffeine* is a useful drug acting on the higher nerve centres, medullary centres, cardiac muscle and coronary vessels But it has a tendency to aggravate restlessness and insomnia It may be given as *cafein sodium benzoas* gr 5 to 7 $\frac{1}{2}$ intramuscularly or very slowly intravenously every six hours *Strychnine* in full doses may be helpful, gr $\frac{1}{30}$ may be given

every three hours but should be stopped if it causes excitability *Digitalis* or *strophanthin* should not be used in cases of peripheral failure Both are definitely harmful in peripheral failure, and quite ineffective even in cardiac failure because of the presence of infection, slow circulation, and inadequate absorption *Adrenal Cortical extract* is useful where there is loss of sodium chloride and water Cortin, Percorten-Ciba or desoxycorticosterone acetate may prove useful in reducing the permeability of damaged capillaries

7 *Intravenous fluids* In traumatic shock, the most important single therapeutic measure is transfusion of whole blood, plasma or serum Judicious use of small transfusions may also help in medical cases Small quantities of hypertonic solutions, 50 to 100 c c of 50 per cent or 25 per cent glucose solution given intravenously twice a day are most helpful In cases of excessive loss of fluid or sodium chloride 5 per cent glucose saline or 300 c c of a 5 per cent solution of sodium chloride may be given intravenously till there is a rise in the venous pressure Large amounts of crystalloids should be avoided in cases of failure where toxins have damaged the capillaries and where there is anoxemia In such cases there is a serious risk of producing an acute pulmonary oedema

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BLOOD TRANSFUSION

A Preliminary Report

By

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The subject of blood transfusion has been already dealt with in great detail in some excellent monographs on the subject and more and more experiences are available to the profession through most scientific journals. However, it is intended to deal, in the present article with some aspects of blood transfusion, which might be helpful in emergency and war-time conditions existing in our own country at the present time. The work in this connection has been and is being carried out at the Seth G S Medical College and the associated K E M Hospital.

In the following paragraphs, I propose to deal with the sources of blood available for transfusion, the selection of donors, a few valuable clinical points regarding matching of bloods, the technique of collection, preservation, and transfusion and some of the common complications.

Sources of Blood

The main sources of blood for transfusion would be the *voluntary donors* of a community including relatives of patients or paid members of a transfusion service. In emergency conditions, it is very advisable to group every person in the city, as apart from the large number of suitable donors available, it would be difficult to foretell who might be the unfortunate victims requiring blood for saving their lives. I might further add, that in emergency conditions, of extreme urgency, *stored blood* from a blood bank should be used rather than fresh blood, as the latter procedure however quickly done, apart from the difficulties of getting suitable donors to a Hospital or collection centres, does take sufficient time during which some patients may pass in a condition beyond the hope of recovery. Secondly, it would take the time of some of the medical and laboratory staff who could otherwise be available for doing other valuable and urgent work. I would further suggest, that blood for banking purposes should be collected from donors not residing near or working in the Hospitals, as these donors, who would be in a comparatively safer area, can be used, if blood, more than the blood bank can distribute or when fresh

blood with all its antibacterial properties is required as for example in combating acute infections. The proportion of stored blood should as far as possible be the same as the ratio of the different blood groups in any place. In Bombay, from an analysis of 789 blood groups in the K E M Hospital the various groups have been found to occur in the following proportions. Group "AB" 7.5%, Group "A" 25%, Group "B" 28%, Group "O" 39.5%.

A small amount of blood for storage would be available from patients suffering from acute pulmonary edema, congestive cardiac failure and hypertension, who would otherwise be free from any other active disease and in whom venesection would be indicated. Placental blood which is very valuable source of blood and should be quite sufficient to meet the requirements of any city in ordinary times, will not be available for emergencies, as the number of confinements in a city would fall considerably owing to the precautionary evacuation of large number of women from cities. The use of cadaveric blood, collected from suitable cases, i.e., those unfortunate otherwise healthy persons who might die a violent or asphyxial death as from head and chest injuries or from internal hæmorrhage, may have to be considered seriously, if unfortunately the casualties in an emergency mount high rapidly. In that case, on an average from 1,500 to 2,000 c.c. of blood would be available from a single cadaver. What is more, this does not require any anticoagulant to prevent it from clotting. But the blood has to be collected within 2 to 3 hours of the patient's death, from the Internal Jugular vein, taking all aseptic precautions as in a surgical operation and the blood has to be given within 10 days of collection.

Lastly, if large quantities of stored blood remain unutilised, the question of plasma transfusion will have to be worked out. This requires a special apparatus. The plasma is collected aseptically in separate bottles and can then be preserved for considerable period of time or may be by a special process of drying converted into a yellowish powder and sealed in ampoules. Such ampoules are being used abroad extensively. Each ampoule contains 20 mgm. of the powder and when mixed with 250 c.c. of sterile distilled water makes a solution equivalent to the plasma of a pint of blood. This is specially useful for shock with little or negligible loss of blood, e.g., shock from burns. It may be added here that plasma too being of four types corresponding to the four blood groups, only Group "AB" plasma containing no agglutinins is ideal for transfusion purposes and can be given in any quantities with impunity. The plasma of other groups containing one or both the agglutinins, should not for obvious reasons, viz., of causing agglutination of the patient's cells, be given in quantities exceeding a pint at a time and should, whenever used, be given preferably diluted with saline and at a very slow rate, about half the usual drip rate, i.e., about 20 drops a minute.

Selection of Donors

In an emergency, as practically every person, I hope, would be grouped, only those members of either sex, who are preferably between the ages 18 and 45 and otherwise healthy, should be chosen as donors. They should be free from venereal disease, active or latent phthisis, nor should they be subjects of high or low blood pressures. Subjects of asthma and those showing allergic manifestations should be discarded. Care should be taken to see that the donors have good elbow veins and it should be a rule not to dissect the veins of donors for collection of blood. Persons suffering from malaria can be treated and then enlisted as donors. The donors should be carefully grouped with high titre sera (the standard used, having at least a titre of 1:100) and cross checked by matching their sera with the cells of a known group. A large number of Group "O" (IV Moss) donors should be kept for emergencies. But those Group "O" donors having a high titre serum should be rejected as their blood contains—both L and P agglutinins in such high concentrations as likely to produce harmful effects on the recipients belonging to other groups. The W R or Kahn test should be done as a routine.

On an average a healthy donor can safely give a pint of blood every $2\frac{1}{2}$ to 3 months, i.e., about 4 to 5 times in a year. He may however attend the calls oftener if lesser amounts of blood are withdrawn. To avoid donors presenting themselves for donating blood frequently, it is advisable to supply each certified donor with a card, wherein besides the details of his group, etc., the *dates* and *quantities* of blood withdrawn are also mentioned. In any case whether he should be bled or not should be decided every time after estimation of his Hb % which should preferably be above 95% and must on no account be below 80%. If below the latter figure, he is prescribed a period of rest and suitable hæmatinics till the anæmia disappears.

Grouping and Matching

In a well equipped Hospital with a pathology department attached to it there will not be difficulties regarding the results of grouping and matching of bloods. But it is not difficult to arrive at the same conclusions for a clinician also. With a little practice, even resident medical officers would be able to do these tests in their ward laboratories. Therefore a few points of importance will be stressed here.

The blood group should preferably be determined by using stock high titre, serum of Group A and Group B, with a titre of at least 1:100 and the group is verified by cross matching with known cells and unknown serum. The result as seen by the naked eye or with the aid of a hand lens may be confirmed by using the low power of a microscope. This is necessary, as, inspite of using the high titre

sera it was noticed that agglutination in some cases is not clearly seen early with the naked eye or the hand lens. Care should be taken to avoid the fallacy of auto-agglutination in cold, occurring in some sera, by previously warming the porcelain tile on which these tests are made, by dipping it in warm water. The donor should as far as possible be chosen from the same group as that of the patient whenever possible, and cross matching test should always be done to avoid the risk to the patient arising from a likely clerical error. But in an emergency, a known Group "O" donor can safely be used taking care to give the blood at a very slow rate.

Collection of Blood

Various methods mostly open, are well-known and are quite adequate where the blood has to be given fresh or at the most within a few hours of collection. But with increasing demands made by emergencies for large quantities of readily available blood, the need for storing blood is keener than ever, necessitating the blood to be collected by a closed and an entirely aseptic method. Personally, I am in favour of all bloods being collected aseptically as apart from the process being very clean even æsthetically, the blood can be stored whenever necessary, the percentage of febrile reactions on the patients are minimised, can be given in fractional doses from the same container when indicated, the collection can be done very quickly, (250 c.c. of blood can be collected within 2½ to 3 minutes) and can be carried out almost single-handed. The method has been used by me and by my colleagues for the past 2 years at the K E M Hospital and I find on going through literature that a similar method is being now employed at the E M S in England. I may also add, that no special or costly apparatus is required for this purpose.

Apparatus Required for collections of blood

1 Two No 15 B D Gauge 2½" to 3" long short-bevelled needles (It is better if one of them is 6" to 8" long in the form of a canula. This directs the blood flow directly on to and just above the anticoagulant fluid in the collecting bottle, and the possibility of formation of minute clots due to blood trickling down the walls of the collecting bottle and hæmolysis of some of the red cells due to forcible impact of the blood flow on to the surface of the anticoagulant is reduced to a minimum, if not completely avoided. Such long needles have been made for us by Powells Ltd.)

2 10" long transparent rubber tubing and a small clamp

3 A hypodermic needle

4 A small piece of rubber tubing (1") with a sterile air filter

5 Blood pressure apparatus

6 A sterilised filtrair bottle fitted with a rubber diaphragm and a metal cap having a large $\frac{1}{2}$ " size central opening in it The bottle contains a known amount of anticoagulant

7 Sterilised towels, iodine, spirit, swabs, dressing and bandages

Articles No 1 to 3 are sterilised and kept ready in a tray The filtrair bottle containing the anticoagulant is sterilised in the following manner The bottle is cleaned and is filled with a known quantity of freshly prepared filtered anticoagulant (This will be considered below) The metal cap with the rubber diaphragm is screwed on but is kept slightly loose The cap is covered over by a piece of gauge and paper and tied The bottle is then sterilised in an autoclave As soon as the bottle is removed from the autoclave, the cap is tightened, so that when the steam condenses as a result of cooling, a partial vacuum is produced and the rubber diaphragm gets drawn in

Anticoagulents

Here again a variety of anticoagulents have been used by different workers Citrate, Transfusol Sulfarsphenamine, Heparin, etc But sodium citrate forms the basis of most anticoagulant solutions in universal use and is the one considered here The minimum concentration of this salt required to prevent the blood from clotting has been worked out to be somewhere between 0.35 to 0.38% Hence, one of the favourite anticoagulant solutions in use is a 3.8% solution of Sodium citrate One part of this solution when used with nine times its quantity of blood gives the desired 0.38% concentration of the citrate in the whole fluid

In the K E M Hospital, I have worked with 2% citrated saline solution 15 cc of this being used for every 100 cc of blood that are to be collected This solution has been used for fresh blood transfusions or when the blood is preserved for a few hours to 2 to 3 days only

For storing the blood, although the 3.8% citrate solution is being used in England, the Russian workers have shown that in the pure citrate solution, as the blood is stored, diffusion of ions especially of Potassium ions takes place from the red blood cells into the plasma This is likely to make the blood more toxic to the patient in course of time and might also interfere with the preservation of the red cells Clinically, however, as no toxic symptoms have been noticed in patients due to diffusion of Potassium ions, in bloods with pure citrate it may be that the concentration of this ion does not reach the level of toxicity However, the Russians

have used and are still using a solution known as the I H T solution (used at the Institute of Hæmatology and Transfusion of Moscow and now used all over Russia and also in some other countries) in which the various ionisable salts are nearly in the same concentration as in the blood, so that their diffusion is reduced to a minimum

The composition§ of this fluid is

Sodium chloride	7 0	Grams
Sodium citrate	5 0	,
Potassium chloride	0 2	„
Magnesium sulphate	0 004	„
Distilled water	1000	cc

This solution* is used in the same quantity as the quantity of blood that is collected. In the K E M Hospital graduated pint bottles containing 250 cc of this solution are sterilised and kept ready and the blood is collected upto the mark of 500 cc

Besides these, there are other citrate solutions, containing in addition, either dextrose or dextrin. The latter substances help to prevent the hæmolysis of the red cells for a much longer time. In these solutions, the dextrose or the dextrin part of the solution has to be sterilised separately from the citrate solution and mixed in certain proportions just before use. This requires a more elaborate technique, for sterilization and is more time consuming. In experience, the results with I H T solution have so far been quite satisfactory and encouraging.

Technique of Collection

The donor, who is advised to come before his meals or a few hours after his last meal, is made to lie on a bed with one of his arms exposed. The cuff of a blood pressure apparatus is tied to his arm and his blood pressure is taken. The cubital fossa is exposed, painted with iodine, the excess of iodine is removed with spirit and the area is isolated with a sterilised towel. No local anæsthetic is required, as the pain amounts to no more than a momentary prick. The apparatus is assembled, as shown in the accompanying figure 1

§ Goodall et al — Surg Gyn & Obst 60 176 1938

* According to other authors, the amount of magnesium sulphate in I H T Solution is 10 times the amount mentioned above (Surgery of Modern Warfare, edited by Hamilton Bailey 1940 P 13 and A Bogdasov in Int abstr Surg Vol 60 p 539 1935)

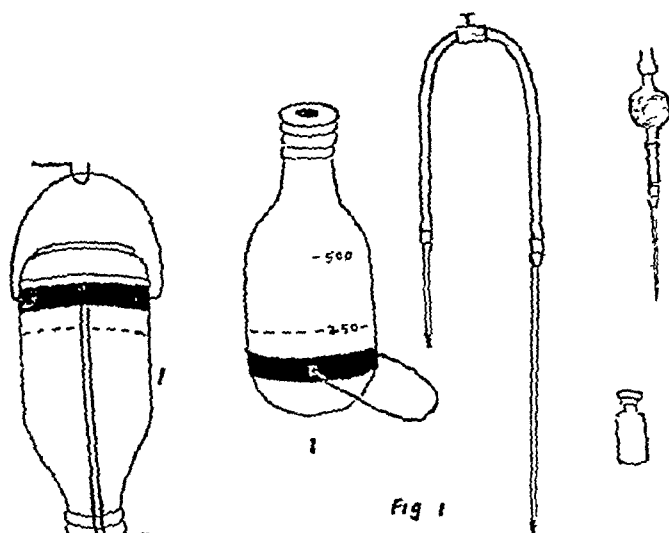


Fig 1

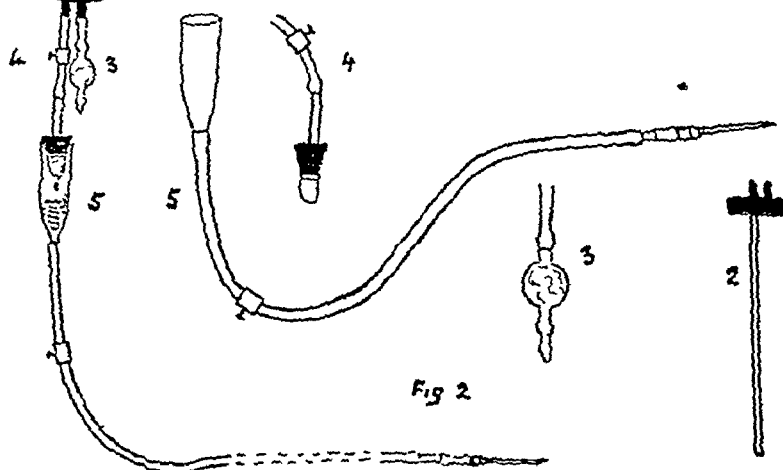


Fig 2

Fig 3

The blood pressure cuff is distended till the pressure reaches the diastolic level usually between 70 and 80 mm of Hg. When the spirit over the cubital fossa has evaporated, a prominent cubital vein is fixed and pierced with the short 3" long needle. Blood begins to flow down the tubing and is seen as the tubing is transparent. Just before it reaches the other end, the rubber washer of the collection bottle, already swabbed with spirit is pierced with the long needle attached to the other end of the tubing till the tip is just above the level of the anticoagulant in the bottle. The blood flows down into the bottle in a continuous stream owing to

the negative pressure in the bottle and syphonage action. But after a time, the flow sometimes slows down, when the rubber washer is pierced at a second spot with the hypodermic needle carrying a sterilised air filter to allow adjustment of pressures within and outside the bottle. The blood flow suddenly improves and in this way 250 cc of blood are collected in 2 to 3 minutes. The cannula in the bottle is withdrawn gradually as the level of blood in the bottle rises. Before removing the long needle from the bottle the pressure in the cuff is released, and the tubing is clamped and then the needle in the vein is withdrawn pressing the site of the puncture with a piece of sterile gauze. The blood in the tubing is let into sterilised test tube or a small 5 cc bottle for grouping and Kahn's test. The needle carrying the air filter is removed from the bottle, the cap swabbed carefully with spirit, covered with a sterile gauze and tied. A label showing all the necessary details including the date of collection, group, etc., is tied to the neck of the bottle, as also the small bottle or test tube containing blood for grouping.

If 500 cc of blood are to be collected, the tube along which blood flows is pinched between the fingers or with a clamp, the needle in the bottle withdrawn and another similar bottle containing the anticoagulant is pierced. The clamp or figures are then released and the blood flows down again into the second bottle. The rest of the procedure is as before. In the beginning, suction was used with a bulb applied to the filter, but with more experience this part of the technique was omitted as its need was not felt.

After the required amount of blood is withdrawn from the donor, his elbow is dressed with sterile gauze and bandaged. Iodine or spirit should not be applied to the site of puncture, as it smarts. He is then advised to rest for a few minutes and is given hot coffee with bread and butter. Instructions are left with him not to remove the bandage for a few hours and to inform the Hospital if he bleeds from the site of the puncture or notices a swelling with bluish discolouration in his cubital fossa.

Preservation of Blood

The bloods so collected aseptically after they are properly labelled are preserved in a refrigerator at 4°C. Shaking should be avoided as far as possible during collection and transit till the time of transfusion. Stored blood left undisturbed settles down within 48 hours in three layers. There is a supernatant lemon yellow coloured layer of plasma, a very small intermediate creamy layer of white cells and at the bottom the scarlet coloured layer of packed red cells. Once it settles down in these three layers it should not be disturbed as it tends to produce hæmolysis earlier than usual. By the end of a week to 10 days, a little reddish tinge is seen just above the layer of red cells. If the tinge is deeper or more diffuse

especially in the first week, infection should strongly be suspected. Such blood should not be transfused under any circumstances. The chances of infection in the samples of blood collected are minimised, if collection is done by one or a few people trained in its technique. More recently Sulphonamide group of drugs in the dose of 20 mgms of the drug to every 100 cc of blood, are being used in different transfusion centres to prevent infection of preserved blood. In my own series, this drug has not been used so far.

Preserved blood should be given if possible within a week to ten days. Some authors (Riddell) prefer to give it within 3 days, others within 2/3 weeks. I have used one sample of preserved blood after it was preserved for 28 days, with definite benefit to the patient. As the blood is preserved, the platelets, white cells and the antibodies are destroyed within 48 to 72 hours. Therefore, blood preserved for more than 3 days helps only in replenishing red cells and plasma proteins. Evidence is also accumulating to show that in blood preserved at 4°C spirochaetes are destroyed within a period varying from 15 hours to 5-5 days, and the chances of syphilis being transmitted to a patient, from blood with a positive W R or Kahn's test are minimised and even practically avoided if that blood is preserved for 5/6 days. This might solve another important problem of getting sufficient number of suitable donors in an emergency.

Indications and Contraindications

The various indications for transfusion, viz., for blood loss from injuries, etc., various types of anæmias, infections, conditions of shock, as an aid to enable the patient to withstand a major operation, etc., are too well known and are therefore not discussed here. But one feels that blood, although it should not be used as a panacea for any kind of disease, can when carefully used and does help to tide the patient through anxious moments. One of the chief guides is the Hb percentage of the patient's blood. If it is between 15 to 25% transfusion is absolutely essential. Upto 45% transfusion is strongly advisable, and for all surgical cases, it is desirable to have a 70% preoperative hæmoglobin level whenever possible. The need for replenishing excess of blood lost during a major operation can hardly be overstressed.

For conditions of shock where blood loss is absent or negligible, plasma transfusions are quite effective and should be preferred. In combating infection as an aid to other measures, when transfusion is indicated, fresh blood should be given in preference to preserved blood. In an emergency, occasions for the use of Serum transfusions may arise especially in shock due to burns, when plasma may not be available. The blood is collected aseptically without any anti-coagulant and is allowed to clot. The supernatant separated serum is then syphoned into a separate container and transfused.

The following contra-indications for transfusion of blood may be mentioned here Kidney diseases, especially the various types of nephritis should be regarded more or less as absolute contra-indications, so also cases of cardiac failure Extremely weak and anaemic patients with a poor myocardium are as a rule bad subjects and if transfusion is given, great care should be taken to see that only small amounts of blood are employed and the blood is administered at a very slow rate

Transfusion

Transfusion can be effected directly from the doner to the patient by means of a special apparatus or indirectly after the blood from a doner is collected in a receptacle Numerous techniques and the modifications of each of these two methods have been devised by different authors and most of them have given excellent results especially in the hands of their originators The various merits and demerits of these methods are not discussed here What matters most is that the blood from a doner should enter the circulation of the patient with little discomfort or reaction to him and the process involved should if possible be simple and efficient With increasing experience in this work, it appears, that in an emergency at any rate, the indirect method will come to be used exclusively With this end in view, a simple efficient and comparatively non-expensive method has been tried out by me successfully at the K E M Hospital and will be described below

Apparatus required

- 1 The filtran bottle containing blood
- 2 Accessory cup
 - If this is not available,
 - (a) 3" long 15 B D Gauge needle
 - (b) 5" long No 18 Gauge needle
- 3 5" long transparent rubber tubing
- 4 1" long transparent rubber tubing
- 5 Sterilised air filter
- 6 Drip arrangement consisting of
 - (a) cylindrical glass funnel, (20 mm diameter \times 2½" long)
 - (b) rubber stopper fitting (a) above and carrying an inlet glass tube and a brass filter
- 7 4' long transparent rubber tubing
- 8 A small glass tube (for a terminal glass window)
- 9 1" long transparent rubber tubing
- 10 No 18 B D 2" long needle with a short bevel or a cannula
- 11 Instruments for dissection of veins
- 12 Sterilised saline
- 13 5 cc syringe with a hypodermic needle
- 14 1% novocain (sterilised)
- 15 Sterilised towels, swabs, etc

*Technique of Transfusion**Premedication*

(1) Before transfusion the patient is given an alkaline mixture 4 times a day, for about 2 days, to render the urine alkaline

(2) One $\frac{1}{2}$ gr Ephedrine hydrochloride tablet may be given by the mouth just before the transfusion

(3) The patient is kept warm

(4) Morphia with atropine and coramine are kept ready So also hot water bottles

The apparatus which is kept sterilised in a tray is assembled as shown in the accompanying figure No 2 (See p 327)

The patient's forearm is exposed, isolated and cleaned with spirit Part No 5 is filled with sterilised saline, all air bubbles are removed and after compressing the patient's arm to make his veins prominent, a suitable vein is pierced with the needle As soon as blood is seen in the glass window, the pressure on the arm is released and the saline is allowed to flow in Parts No 1 to 4 are assembled as shown on figure No 3 with the clamp on part No 4 tightly closed The funnel is filled with saline and as the level drops by one fourth, it is connected to the rubber stopper as shown in the figure, the clamp on part 4 is then gradually released and blood begins to flow down into the drip, which is then adjusted at the required rate

Rate of flow

The blood should always be started at a very slow rate and in patients who are otherwise in good health, e.g., accident and injury cases, about 500 cc may be given in 10 to 20 minutes When transfusion is given during the operation, the rate should be adjusted according to the blood loss and the condition of the patient's myocardium The average rate is between 40 to 80 drops a minute In weak and anaemic patients with poor myocardium, blood should be given preferably in small quantities, 100 to 150 cc and at a very slow rate, 10 to 20 drops per minute

There is no need to warm the blood before transfusion in a very urgent case In this city by the time blood is removed from the refrigerator and the parts are assembled, it becomes sufficiently warm and no bad effects are seen especially if it is given by the drip method For a rapid transfusion, the blood may be brought nearly to body temperature by leaving the bottle in a bowl of warm water with a temperature of 38°C for 15 minutes But under no circumstances should the temperature go above 40°C as it may cause some disintegration of the plasma proteins—and may produce a severe rigor

When all the blood goes in, the clamp on part No 4 is closed and part No 5 is detached. Saline is now poured in it and all the blood in the tubing is allowed to pass into the patient's body. The needle is then removed and the part dressed.

The transfusion should be done preferably in a quiet place and the patient is encouraged to go to sleep. If necessary, he may be given an injection of morphia or omopon.

Complications

Here also, only those complications which have been commonly met with will be discussed. Complications due to gross incompatibilities of blood described at length in different books should never occur, if proper care is taken in matching the bloods.

The commonest reaction seen as a result of transfusion is the *Pyrexia* varying from a slight rise of temperature to a chilly feeling and even a regular rigor. Various causes have been attributed to this in the past, e.g., excess of citrate, too rapid transfusion, transfusion of cold blood and so on. But it is now known definitely that the majority of these rigors are due to injection into the patient's system of foreign protein substances derived either from air borne contamination of blood or the solutions by bacteria, microscopic portions of dried blood clots sticking to the walls of the tubing due to inefficient cleansing before sterilization. In others it may be due to technical faults in the collection of blood, e.g., the blood flow may be directed to the walls of the container or may be intermittent, as a result of which, minute coagula may form. At times it may be due to want of temperature control leading to autoagglutination in the cold. Very rarely, from minor incompatibilities of blood arising from the use of universal donor with a high titre serum, or accessory agglutinins or idiosyncrasy. Most of these cases can be eliminated by proper selection of cases and a sound transfusion technique. Rapid transfusion may account for an occasional rigor.

The treatment of this febrile reaction is mainly prophylactic as outlined above, and if a rigor does occur, the transfusion if not completed should be stopped. The patient is given hot water bottles and an injection of adrenaline $\frac{1}{2}$ cc. If it is very severe morphia gr $\frac{1}{4}$ with atropine gr $\frac{1}{100}$ is given as well.

Urticaria is seen at times. I have seen it only twice in the last 80 cases. It manifests in the form of a wheal and was seen on the forehead and face in one case and on the forearm on the side of the transfusion in the other. This may be due to the patient's sensitivity to any substance circulating in the donor's blood or a donor with an allergic taint. These can be avoided by proper selection of donors and the prophylactic use of Ephedrine, before transfusion is begun. If urticaria does develop, an injection

of $\frac{1}{2}$ cc adrenaline is given and then repeated in 1 min doses till it disappears

Discomfort in the chest in the retrosternal region and occasionally cough I had this experience only once and this was probably due to transfusion being done rather rapidly. However, it may occur in patients with poor myocardium even if the transfusion is done at the usual drip rate, i.e., 40 drops a minute. It is said to be due to the right heart not being able to cope up with the large venous return. The treatment is mainly prophylactic. If it does occur, the rate of flow should be slowed down and may have to be stopped. Cardiac tonics may have to be employed in addition.

Summary

- (1) The salient features of blood transfusion as would be applicable to emergency conditions, in this city at the present date are considered
- (2) A plea is made to use "stored blood" in an emergency as far as possible except when dealing with infective conditions
- (3) A simple and efficient method of collection of blood and transfusion has been described
- (4) The common complications have been discussed

I wish to thank Dr Jivraj N Metha the dean of the K E M Hospital and Dr R G Dhavagude Professor of Pathology for giving me the necessary facilities to carry out this work and the various members of the Hon Staff of the Hospital for allowing me to do the transfusions on their cases. My special thanks are due to Mr S M Nadkarni of the Pathology Dept. of the College who has helped me considerably in perfecting the technique and for other valuable suggestions.

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TREATMENT OF BURNS IN THE ROYAL AIR FORCE

1 A burn is a toxic wound which results from a thermal, chemical or electrical agent. It may be associated with certain complications or sequelae which either threaten the life of the patient or, if he lives, permanently disables him. These general and local effects are—

- (a) Shock
- (b) Toxaemia
- (c) Sepsis
- (d) Scarring with deformity

Hence treatment is directed to the saving of life, the healing of the burned areas and the preservation of function in the parts burned. These three aspects are most easily described in separate sections, but it must be borne in mind that they are in reality a single problem. The local treatment must be designed and carried out so that it will neither prejudice the general condition nor the ultimate function in the parts involved. General treatment must have in view the early control of shock, toxaemia, and sepsis, which menace the patient's life, so that the restoration of function will not be delayed.

2 In the R A F the problem of burns is a special one because the causes of burns, the location and extent of the burns, the age-group and general condition of the patient all differ from those seen in the civil population. The causes of R A F burns in order of frequency are—

- (a) flame burns from blazing petrol
- (b) burning by liquid petrol and/or glycol on the skin
- (c) incendiary bomb flash and other fire burns
- (d) phosphorous burns
- (e) electrical burns

As a result, exposed areas of the body of functional importance are burned, notably the hands and face (80 per cent) and there is a higher incidence of encircling burns. These burns occur in fit young men in these situations. This is in contradistinction to civilian burns, which occur in the very young, the unfit and the aged, and are usually body burns due to boiling water, steam or fire.

3 *Phosphorous Burns*—These result from self-igniting phosphorous grenades, etc. Small particles of phosphorous remain buried in the skin and continue to burn. They must be promptly dealt with and the particles removed (paragraph 39).

4 *Electric Burns*, are of two types—

- (a) Those produced by an accidentally produced circuit
- (b) Those produced by passage of an electric current through the tissues which are heated by the passage of the current (Joule effect)

These burns appear as yellowish grey lesions, sharply demarcated from the surrounding skin, slightly depressed and densely adherent to the subcutaneous tissue. Toxaemic symptoms do not occur and there is little inflammatory reaction. Healing is very slow and the treatment does not differ from burns from other causes.

5 *Diagnosis*—From the practical standpoint, it is essential to distinguish between a partial and a complete skin loss. In the former, rapid regeneration of skin is possible, in the latter, it is not. (For this reason obliteration of the diagnostic points by coagulation therapy, applied at Station Sick Quarters before the case is transferred to a Burn Unit, is inadvisable.) The diagnosis between them is easy at the two ends of the scale, i.e., between erythema with mild blistering, and charring or splitting of the whole skin down to the subcutaneous tissues, but it is difficult in that common type of case where severe second degree burns closely resemble third. Examination of the exposed dermis may decide the point. Any sign of dermal circulation, however slight, may mean that the depths of the papillae have escaped. Blackened, wrinkled epidermis, hanging from an opaque, yellow-white dermis, usually means a third degree burn with complete skin loss. Slight pressure on the dermis may produce blanching of the surface or bleeding may follow gentle rubbing. If either of these signs is present a partial skin loss is presumed. The matter is made more difficult by dirt, oil or first aid dressings, particularly of the coagulative type. Burns deeper than whole-thickness skin destruction naturally occur, and at the same time the presence of an area of heat-fixed tissue beneath the layer of absolute destruction must be born in mind. This must influence prognosis in certain areas e.g., hands, face, flexures, etc., but the treatment is the same as for whole thickness skin loss.

6 *Prognosis*—The outlook for life and subsequent function depends on the extent, depth and location of the burn. While burns of great extent are dangerous to life, those of lesser area may have no lethal meanings but instead may seriously affect the function of the part involved. Thus an extensive burn of the trunk may put the patient's life in jeopardy, but when healed, even with bad scarring, may leave him without serious disability. On the other hand, loss of a piece of skin the size of a postage stamp on the lower eyelid may produce rapid entropion with exposure of the globe, corneal ulceration, perforation and blindness. Again, the most crippling deformities of the hands may follow deep burns of small extent which give rise to no anxiety whatever so far as the patient's life is concerned. The prognosis for function, therefore, depends largely

upon the depth and location of the burn. The outlook for life, on the other hand, is determined more by the extent of the burn than by its depth or location, for shock and toxæmia are directly related to the total area of skin involved. Any burn exceeding 25-30 per cent of the body surface must be viewed with concern. Patients with areas up to 60 per cent may survive and others with as little as 10 per cent may show severe shock. This is largely a matter of individual variation. The area involved may be easily estimated by reference to Berkley's Chart. Burns of the anterior surface of the chest and the abdominal surface (20 per cent) are far more dangerous than a corresponding area on the back. Burns of the face and head (3-6 per cent) are often associated with quite severe shock and toxæmia. The extent of the burn must also influence treatment, for therapy is imperative, though this may not be advisable with smaller, but deeper burns in special areas. Treatment and prognosis must be based, therefore, on a careful diagnosis of the depth of the burn, its extent and location in relation to the immediate danger to life, and the remote possibility of functional disability.

The Preservation of Life

7 This may be a matter of extreme urgency and must receive instant attention. It depends on the control of (a) shock, (b) toxæmia, (c) sepsis.

8 *Shock*—This has been divided into primary and secondary, the former resulting from vasomotor disturbance following injury, from asphyxiation and blast, and the latter from the chain of pathological events due to the burn itself. In burns of wide extent the two may be indistinguishable and death usually results. Primary shock is characterised by a fall in blood pressure, feeble pulse, clammy skin and subnormal temperature. When the patient is given the usual simple anti-shock remedies (rest, warmth and morphine) the blood pressure usually returns to normal within a few hours. In many cases the condition passes insensibly into secondary shock.

9 *Secondary Shock*—This is the chief cause of death after burns and accounts for 80 per cent of fatalities. It is directly related to the surface extent of the burn rather than to its depth, and is more marked with lesions of the anterior surface of the trunk than those of the back or extremities. The mechanism of secondary shock is related to loss of plasma from the circulating blood, on the surface and into the tissue spaces of the burned and unburned areas, through the walls of the injured capillaries. The circulatory volume of blood is reduced and becomes concentrated, the output of the heart decreases, and ultimately, in spite of compensatory processes, the blood pressure falls. Reserves of tissues fluid deficient in protein pass back into circulation, thus lowering the concentration of protein in the plasma. When this compensatory mechanism fails, concen-

vation of the blood becomes more marked with rising haemoglobin percentage and colour index, and increasing erythrocytes per cubic mm in the peripheral circulation. In the average case involving the hands and the face, Hb rises to 106 per cent and the erythrocytes to 6 millions. An increase of Hb to 120 per cent, and the erythrocytes to 7 millions demands immediate and energetic treatment, while a rise of Hb to 140 per cent and erythrocytes to 9 millions in spite of adequate treatment is of grave significance. There is usually a leucocytosis of 20,000—30,000. A fall in the blood chlorides is also noted. Eventually irreparable damage is done to vital structures such as the heart and the CNS, when failure becomes irreversible. Clinically, it is often difficult to detect the early signs of developing shock, but the following are suggestive: decreasing pulse pressure (the difference between systolic and diastolic levels), increasing pulse rate, thirst, restlessness and increasing concentration of the blood as shown by Hb and erythrocyte estimations. Established shock is characterised by lowered systolic B.P., rapid feeble pulse, rapid shallow or irregular breathing, restlessness, or apathy, thirst, vomiting, greyish pallor and usually subnormal rectal temperature.

10 *Time of Onset*—This is usually one to five hours after injury, but may be delayed for twenty-four hours. It may occur in one of three distinct periods:

- (a) As an extension of primary shock,
- (b) during the course of local treatment, particularly as a result of loss of fluid, exposure to cold, merciless cleaning of the burns with scrubbing brushes, ether, soap, etc., and the use of depressant anaesthetics such as ether and chloroform,
- (c) following local treatment and probably a delayed action from (b).

11 It is obvious that the delicate circulatory balance is easily upset, especially by local treatment. Emphasis is therefore laid on the absolute necessity for gentle handling of burned patients, for strict adherence to certain rules of local treatment, and for a watchful attitude on the part of the medical and nursing staff to anticipate, if possible, the occurrence of shock.

12 *Acute Toxicæmia*—The cause of this is still in doubt, and has been ascribed, (a) to a toxic product derived from the autolysis of the burned tissue which produces general degenerative changes most marked in the liver, (b) to infection, particularly by a hæmolytic streptococcus, (c) to fluid loss and concentration of the blood. The weight of evidence supports the view that a specific toxin is produced at the site of the burn which is absorbed into the general circulation. Like secondary shock it is more common with extensive than with deep burns, but unlike it, may show no evidence of concentration of the blood or bacterial infection.

13 *The clinical signs* are those of a severe intoxication, apathy and listlessness, or restlessness followed by delirium, vomiting (sometimes of the "coffee ground" type), pyrexia with rising pulse rate, cyanosis or pallor, and other signs of circulatory failure such as decreasing blood pressure. Albuminuria is common. Oedema of the burned area occurs rapidly and there is considerable loss of tissue fluid from the denuded surfaces. The tissue fluid shift also extends well beyond the burned area and there is a tendency towards oedema throughout the whole body. It is of practical importance, apart from its general significance, in the hands where the limiting effect of a rigid tannic casing may produce pressure effects upon the fingers.

14 *The Time of Onset* may be six-to sixty hours after injury, but it is usually between the twelfth and twenty-fourth hour. It may follow controlled shock with a definite time lag of several hours. It may be fulminating.

15 *Sepsis*—Bacterial infection is fairly easily prevented in 1st and 2nd degree burns, provided careful cleansing and coagulation of the burn is undertaken as soon as possible after injury, and after care is adequate. The use of chemotherapeutic agents applied locally and taken internally has also materially diminished its incidence. Nevertheless, under war conditions a high percentage of cordite and bomb flash burns as well as petrol burns may rapidly become septic, whatever the initial cleaning treatment. As sepsis is definitely related to the depth of the burn it is difficult to exclude in severe 2nd degree and definite 3rd degree burns. It would not be an exaggeration to say that 80-100 per cent of 3rd degree burns become infected, particularly beneath a tannic acid coagulum. In well cared for 1st or 2nd degree burns this is rarely seen, and if so not before the second week, but in neglected cases it may appear within twenty-four hours of injury. The usual organism is a haemolytic streptococcus, but staphylococci, coliform bacilli and diphtheroids are also found. These infections are introduced either from the patient's own skin or by external contamination from flies, carelessly applied first aid dressings, inadequately tanned surfaces and through moist coagula. When coagulation therapy is employed the site of entry is the edge of the burn at points of separation of the coagulum and at areas of slow blister formation. In deep burns bacteria may invade the layer of exudate which intervenes between the growing granulation tissue and the necrotic burned tissue, liquefaction of the exudate, softening of the sloughs and active suppuration may follow and if infection is virulent, septicaemia and pyaemia supervenes. The importance of sepsis in healing is therefore great, and the likelihood of its occurrence taken in conjunction with the depth and situation of the burn are in fact, the outstanding consideration in deciding what type of treatment should be adopted. It may be noted in passing that the tanning of 3rd degree burns is allied to the evil practice of primary suture without drainage of infected war wounds.

Subsequent Function in Relation to Depth of Burn

16 The end results of partial skin losses (1st and 2nd degree burns) are excellent, provided sepsis is excluded, since healing occurs by regeneration of epithelium from multiple focal points within ten to twenty-one days. Scar tissue contraction is absent and deformities do not occur. Third degree burns involving the entire thickness of skin, mixed 2nd and 3rd degree, or 2nd degree converted to 3rd degree by sepsis or pressure under a coagulum must result in raw surfaces as soon as the slough has separated. Judging by their incidence, these make a formidable group of cases and can result in the most crippling deformities. This is unfortunately true of the two areas most exposed to burns in war time, e.g., the hands and face. In terms of personal suffering, deformity and disfigurement, strain on the nursing staff and economic loss to the community, few injuries can compare with them. The problem here is the early re-epithelialisation of a raw surface in which multiple focal points are absent and in which the epithelial response from the edges of the lesions is deficient, due to sepsis, poor underlying vascularity and the depressed general condition of the patient. Heat fixation of the periarticular ligaments and tendon sheaths does much to limit joint movement, but if the joints and tendons are allowed to consolidate in the dense basic scar tissue of a granulating surface, permanent joint immobility results. The eyelids retract rapidly, exposing the cornea to external trauma, teeth are exposed by contractures of the lips with serious effects on the necks and enamel surfaces. Contraction bands across flexures produces the deformities wellknown in every orthopaedic department.

The Advantages of Coagulation Therapy in Burns of the Body

17 There is no doubt that coagulation of the burned area, however achieved, is remarkably successful in extensive burns associated with shock and toxæmia, particularly those of the 1st and 2nd degree. The immediate mortality rate is lower, loss of tissue fluid is prevented, toxæmia is largely controlled, multiple dressings are avoided, and rest to the part and to the patient as a whole is obtained. If sepsis is excluded epithelialisation occurs from multiple points beneath the coagulum.

The Disadvantages and Dangers of Coagulation Therapy in Burns of Special Areas

18 Coagulants, such as Tannafax, used as dressing at First Aid Posts on burns of the face and hands have long been advocated. Experience shows however, that they are usually applied hurriedly and inadequately over uncleansed burned surfaces, whatever the degree of the burn and that they compromise the final diagnosis, cleansing and treatment undertaken at hospital. It would be better

If a simple primary application such as "tulle grass,"* a saline dressing covered with a waterproof material, or a water soluble jelly containing sulphonamide was substituted. Any of these can be easily removed and the burned areas inspected and treated under more satisfactory circumstances

19 When tannic acid preparations are used in the treatment of encircling burns of the hands (a type particularly common in the R A F) the following series of events has been noted —

- (a) Limitation of movement of the finger joints beyond what should be expected as a result of the burn itself. The fingers are fixed in flexion during the time the crust is in situ. Not infrequently weeks elapse before this is removed and it may be months before the patient can make a fist. This has been encountered even in 2nd degree burns and where pressure effects are absent.
- (b) Pressure effects. When tannic acid is applied in the pre-dema phase, pressure develops beneath the encircling coagulum. If sepsis occurs the oedema and pressure are increased and the fixed crust fails to yield with increase in the size of the hand. Consequent embarrassment of the digital circulation may lead to spindling of the fingers, partial necrosis of the skin, or even total loss of the digits. A common complication is pressure necrosis of the tissues overlying the proximal interphalangeal joints with perforation into the joint cavities. This may be superimposed on the lesions often seen at those sites resulting entirely from the burn itself. With fixation of the joints and tendons a clawed, useless hand results. It is not fully appreciated that this chain of events can occur in burns of the 2nd degree and that many of these are converted into third degree purely by pressure.

20 On the face difficulties largely centre round the eyes and eyelids and are most marked in burns of the 3rd degree. Pressure effects are not noted but the horny layer of tan on the eyelids may cause great difficulty is where the eyes are damaged and require treatment. If the burn is 3rd degree sepsis is inevitable and rapidly developing ectopion with exposure of the globe, corneal ulceration and perforation may occur beneath the coagulum.

* "Tulle grass," originally a French preparation, may be prepared in the following way. Curtain net, with a mesh of 2 mm is cut into pieces 9 cm square, these are placed in a box of slightly larger size with grease proof paper between each square of material. The box is then filled with the following mixture —

Soft paraffin	96 gms
Balsam of Peru	2 "
Halibut oil	2 "

sufficient to impregnate and cover the material completely after sterilization.

21 The use of tannic acid on 3rd degree burns generally is not advocated unless the control of toxæmia makes its use imperative. Only the superficial layers of the slough are tanned, while the deeper untanned areas must autolyse and separate as best they may. Septic absorption is not prevented and, in fact, is markedly increased since sepsis of varying severity occurs in almost every case. A longer period than is necessary elapses before the sloughs separate and the preparation of the underlying granulating surface for grafting is greatly delayed. Infection becomes thoroughly established in the granulations and their blood supply poor owing to the increased density of the basic scar tissue layer. The epithelial response from the edges is deficient or absent. During the period of closed sepsis there is a steady decline in the morale and stamina of the patient. This is possibly not so unfortunate if the tanning contributed to the prevention of shock and toxæmia, but if neither of these factors is in evidence better results can be obtained by other means.

Treatment of Burns at Station Sick Quarters

22 *Emergency Treatment by the medical officer on the aerodrome*—Having extricated the injured man the medical officer should exclude the presence of other injuries, such as fractures, hæmorrhage or internal injuries, and ascertain what previous treatment has been given. If the burns are uncomplicated and no first aid has been given, he should proceed as in paragraph 26, unless the distance to the Station Sick Quarters is so short as to make any delay undesirable. Complications should be given treatment according to the indications. In all cases the patient should be transported as soon as possible to Station Sick Quarters, where any further emergency examination or treatment can be undertaken. It is highly desirable to transfer burn cases from there to the nearest Burn Centre without delay so that the final treatment can be applied. This transfer can be effected by road or air ambulance.

23 *Minor Burns*—These should be gently cleansed with soap and water followed by saline, and one of the following treatments applied.

- (i) Painting with 2 per cent gentian violet
- (ii) Painting with triple dye *
- (iii) Sprayings with 20 per cent tannic acid
- (iv) Spraying alternatively with 5 per cent tannic acid and 10 per cent silver nitrate
- (v) Gentian dye jelly
- (vi) Tannafax

Care should be taken to protect the resulting coagulum from external infection, and any redness of the skin at the edges should be painted with gentian violet. The patient may be ambulant

* Brilliant Green 1 400, Gentian Violet 1 400, Neutral Acriflavine 1 1000, equal parts of each.

24. Major Burns without Shock—After the preliminary general treatment already outlined in paragraph 28, these cases should be transferred forthwith, whenever practicable, to the nearest Burn Centre

Beyond the application of saline packs or the dye jelly to exposed parts such as the hands or face, no local treatment is to be used and the patient need not be undressed. In particular tannic acid, silver nitrate and coagulant dyes should be avoided as they may seriously compromise the final treatment at the Burn Centre. **ON NO ACCOUNT MUST THE HANDS BE TANNED**

25. Major Burns with Severe Shock—Shock is of paramount importance and must be given instant attention. In these cases the Medical Officer must treat the shock first and apply only first aid treatment to the burns

Treatment —

- (i) Keep warm in bed, preferably beneath a shock cradle
- (ii) Raise foot of bed
- (iii) Give morphia freely, with due regard to previous dosage
- (iv) Give hot fluids freely by the mouth or rectum. Intravenous saline is contra-indicated as it has only a transient effect on concentration of the blood and rapidly passes out into the tissues
- (v) Oxygen may be given by means of the ordinary service mask or through an anaesthetic mask. The B L B mask may be used where available. High concentrations of oxygen up to 10 per cent are advisable
- (vi) Intravenous, reconstituted, dried human serum must be given in all cases of shock as soon as a supply of this becomes available
- (vii) First aid treatment of the burn should consist of the application of special burn jelly

Apparatus required for Administration of Reconstituted Dried Serum

26 (i) Dried Serum—This will be applied in screw-capped bottles each containing the dried products of 200 cc human serum. The bottles should be stored in a cool, dry place but need not be refrigerated. They must not be opened until actually required for use. The contents can be kept indefinitely without deterioration, but when prepared for use must on no account be stored in liquid form

- (ii) **Sterile, doubly distilled water**—This is supplied in 100 cc bottles or ampoules

- (iii) 10 cc or 20 cc glass syringe fitted with 2 way stopcock and intravenous needle The whole must be boiled and cooled before use
- (iv) Rubber tubing, 12 inches, to fit on the side tube of the 2 way stopcock The tubing should be boiled and allowed to cool before use

27 *Preparation of the serum*—The contents of one ampoule of distilled water (100 cc) is added to one bottle of dried serum under aseptic precautions Solution is aided by gentle agitation, or by standing the bottle in a basin of warm water the temperature of which should not exceed 35° Centigrade (95°F)

28 *Technique of Administration*—The syringe is fitted with a 2-way stopcock and needle The rubber tubing is attached to the side nozzle of the stopcock, the other end being led into the serum syringe, after which it is ready for use Injection is made into the antecubital vein by filling the syringe from the bottle, turning the stopcock and injecting the contents into the vein, care being taken to exclude all air bubbles

29 *Dosage*—A minimum of two bottles of double strength serum (i.e., 200 cc actual fluid) should be administered as early as possible If no major improvement occurs in half an hour the dose should be repeated as often as necessary Anaphylactic reactions are extremely rare

Phosphorous Burns

30 Medical Officers may be called upon to give treatment for phosphorous burns resulting from accidents met with in dealing self-igniting phosphorous grenades, etc Particles of phosphorous become embedded in the skin or deeper tissues and continue to burn unless rapid action is taken It is recommended that these burns should be dealt with on the following lines —

- (a) Immerse the affected part in water, or if sufficient water is not available apply a thick pad soaked in water
- (b) Particles of phosphorous embedded in the skin should be removed under water by means of gauze held in forceps
- (c) No oils or greasy dressings should be used
- (d) Wash with diluted alkaline solution, e.g., soda bicarbonate or sodium carbonate, 2 drachms to a pint of water
- (e) Remove all traces of phosphorous by washing with 1 per cent solution of copper sulphate
- (f) Remove resultant dark deposit of copper phosphide and wash with a mild antiseptic, e.g., boric acid
- (g) Dress as for ordinary burns

Disposal Instructions

31 Cases of severe burns may occur leaving the medical officer in doubt as to the best method of treatment and/or disposal In

such cases the opinion of a consultant or specialist should be sought through the most direct channels, without delay

The Treatment of the Burned Areas

32 In almost all cases this will be undertaken in the Burn Centres and not in Station Sick Quarters

The Treatment of Major Burns in R A F Hospitals and Burn Centres.

33 *Treatment of Shock*—The patient is immediately admitted to the Shock ward, and, unless it has been already done, morphine gr 1/3 administered if necessary. The clothing is removed or cut away and the extent of the burn estimated. He is placed inside the shock cradle and the foot of the bed elevated. The temperature, pulse, respirations and blood pressure are taken every hour and charted. A sample of blood is removed and the Hb estimation, red cell count serum protein and haematocrit estimations carried out forthwith. If the burn is extensive and shock is feared or symptoms of shock are already manifest an infusion of reconstituted dried serum is given at once before any local treatment is carried out (see paragraphs 26-29). The amount given at Station Sick Quarters should be noted. Human plasma is used in the same way. There does not appear to be any difference in the action. The minimum initial dose for the former is two bottles of double strength serum (i.e., 200 ccs actual fluid), of the latter two bottles normal strength plasma (i.e., 400 ccs actual fluid). The amount used depends on the condition of the blood. This can be judged by daily or twice daily Hb red cell count, serum protein and haematocrit estimations. Twice daily injections may be given for three days, but as many as 12-15 bottles have been used in severe cases.

34 If the symptoms of shock have progressed to cyanosis of the finger tips and/or lips, and other evidence of tissue anoxia, oxygen administration in high concentration may be resorted to. This is given by means of the B L B Apparatus or by a modification of the ordinary high flying oxygen mask.

(a) The B L B Apparatus consists of a mask and connecting device which joins the mask to the reservoir breathing bag and so to the oxygen cylinder. By adjustment of the air regulating mechanism different amounts of atmospheric air are mixed with oxygen in the inhalation apparatus. As concentration of 80-90 per cent of the oxygen are usually required the apparatus must be used with all the ports closed but the flow should be adjusted so that the bag does not collapse completely before the end of inspiration, or the patient will obtain all his inspired air from the bag.

(b) The Service Respirator is used in the following manner. The apparatus consists of an oxygen cylinder with fine adjustment valve, an oxygen flow meter, rubber tubing, a 1 mm

bore transfusion needle, together with the patient's own standard anti-gas respirator. To utilize this apparatus for the administration of oxygen the respirator is worn in the normal manner and the transfusion needle is inserted, through the corrugated tab, to which it can be affixed by thread or tape. The oxygen is turned on so as to give a flow of 6 litres per minute which should meet normal oxygen requirements. To give pure oxygen a rubber rebreathing bag from the anaesthetic set may be substituted for the container of the respirator, and will act as an oxygen reservoir.

35 *Dehydration*—This contributes to shock and most cases show water and chloride depletion. Hence all burn cases should be encouraged to drink freely. The drink should contain a half-teaspoonful of salt to the pint. This will increase thirst and automatically increase the intake of fluids. The rectal route may be used, but intravenous saline in burn shock should be avoided, as its effect is transient and may do more harm than good owing to its failure to control the concentration of the blood. Later, when plasma and serum have brought this to normal, intravenous saline and glucose may be freely used.

36 *Treatment of Toxaemia*—This is largely preventive, and is directed to the control of sepsis and the fixation of toxic products in the burned area. Coagulation therapy is the established method of dealing with it. Since this is intimately concerned with the local treatment of the burned area, the details will be considered later. Throughout this phase the blood concentration and volume must be maintained by administration of serum or plasma.

37 *Local treatment of the burned area*—As soon as the general condition permits, this should be carried out in a well equipped and specially heated theatre so that when the patient is exposed cooling will not occur. It should frequently be possible to combine the treatment of shock with that of the burned areas so that time will not be lost in unnecessary manipulation.

38 *Anaesthesia*—Morphine and atrophine premedication followed by gas and oxygen is the method of choice, but if burns of the face preclude induction by this method, a preliminary injection of pentothal is followed by the introduction of an intratracheal nasal tube.

39 *Preliminary cleansing*—Exposing the burned area bit by bit, the burns and the surrounding skin are cleaned with great gentleness. The use of a scrubbing brush or of any form of strong antiseptic is to be rigidly avoided for reasons already given. The surrounding skin is first cleaned with soap and water, and the entire area gently swabbed with gauze soaked in saline. Loose pieces of skin are removed and blisters snipped to expose the underlying dermis.

Occasionally oil and dirt can be removed only with difficulty, and here, if shock is not a feature, ether may be used as a solvent. Benzine, if procurable, is an equally good solvent and is less cooling to the patient. At this point a careful estimate is made of the depth of the burn, its situation and extent and the probability of toxæmia and sepsis. As a result the local treatment is decided on. It may take the form of—

- (a) Coagulation therapy
- (b) Saline packs and or baths throughout
- (c) Saline treatment followed by coagulation

In conjunction with all these methods sulphonamide therapy has proved indispensable as an adjunct to the treatment of sepsis.

40 *Control of sepsis*—This depends on (a) early and adequate cleansing, (b) careful attention to detail in the handling of burned patients so that contact with infected articles such as blankets, etc., is avoided. A strict technique should be adopted in ward care. (c) Sulphonamide therapy. This should be given —

- (i) internally in the doses of 2 gms every 4 hours for 24 hours
- (ii) externally in powdered form, directly on the burned surfaces (See paragraphs 56, 57 and 58)

41 *Coagulation therapy*—This can be brought about a number of agents, some of which produce a hard crust, others a softer, more yielding coagulum. All of them have in common the fixation of burned products and the production of a dry, unbroken surface through which tissue fluids cannot be lost nor bacterial invasion occur. The most commonly used coagulants are —

- (a) Aqueous solution of tannic acid 5-20 per cent
- (b) Tannic acid 5 per cent and silver nitrate 10 per cent used alternatively
- (c) Silver nitrate 10 per cent alone
- (d) Vital dyes (aniline)—Gentian violet 2 per cent, triple dye, mercurochrome 2 per cent

The one best adapted to the particular areas is selected for use.

42 *Indications for tannic acid and or silver nitrate*—Extensive first and second degree burns of the trunk and non-encircling first and second degree burns of the arms and legs. Reasonably small areas of third degree loss occurring in mainly first and second degree burns may be included.

43 *Contraindications*—(a) Burns of the face, hands and feet, flexures, perineum and genitalia of any degree. (b) All extensive third degree burns.

44 *Technique*—Coagulation may be either by the quick or slow method. The first is valuable in time of stress, and where many cases are being treated. It produces a satisfactory coagulum which appears to be as efficient as a crust slowly produced. The burned

areas are daubed or sprayed with aqueous solution of tannic acid 25 per cent or alternately with tannic acid 5 per cent and silver nitrate 10 per cent. The surface is allowed to dry and the edges painted with gentian violet 2 per cent, and any fissures or cracks similarly treated from time to time. The patient is nursed in a tented bed containing heating elements and every effort made to preserve a dry, unbroken surface. Minor degrees of sepsis can be controlled by gentian violet painted on the affected areas after removal of overlying crust, but if the entire surface became infected the tan must be removed by soaking in saline packs or in a saline bath.

45 In the slow method tannic acid $2\frac{1}{2}$ per cent is used, the areas being sprayed every twenty minutes for 12-23 hours until a satisfactory coagulum is obtained. It entails much work and handling of the patient at a time when rest is important. Experienced workers find no advantage in it.

46 *Retanning*—If it fails to achieve its purpose in the first instance by reason of subjacent sepsis, it will not be successful by substituting a fresh coagulum following the removal of the crust. *Retanning, therefore, should not be undertaken.*

47 *The Vital Dyes*—(Gentian violet, triple dye, mercurochrome) The aniline dyes have recently found great favour in the treatment of burns. They are efficient coagulants and have the added advantage of forming a softer, less resistant crust which is at the same time antiseptic. The initial cleansing does not need to be so far reaching. They have a more general application than tannic acid but are better avoided in those special areas where function is of importance.

48 *Technique*—The burned areas are painted with dye which is allowed to dry. A single layer of 2 inch ribbon gauze laid in strips over the burn is then painted with another coating of dye and this is in turn dried. This forms a dressing which requires no further attention with the exception of an occasional application of dye at the edges or where moist spots appear. After ten to fifteen days the gauze dressing is spontaneously shed or can be removed. In most cases the burn is found to have epithelialized over, but as the new skin is still delicate and easily traumatized, an occasional painting with the dye is advisable.

49 *Saline sulphonamide treatment*—The indications for the use of physiological saline in the treatment of burns are as follows—

- (a) Ab initio treatment of all types of burns involving the face, hands and feet, flexures and perineum
- (b) Ab initio treatment of third degree burns in any area
- (c) For the removal of tannic acid or other coagula with underlying sepsis

- (d) For the preparation of all raw surfaces requiring skin grafting

50 *Saline—Sulphonamide treatment in special areas*—The hands or feet are immersed in small baths containing normal saline at 97° F. The patient is encouraged to move his fingers and wrist joints, or the toes in the solution. Two or three baths of one hour each are given each day. Following each bath and without allowing the affected areas to dry, they are covered to a depth of 1/64 inch with sulphonamide powder, using a suitable pump or hand dredger to spread the drug evenly. This in turn is gently covered with tulle grass and several layers of gauze soaked in warm saline laid upon it, without pressure, so that the saline can trickle on to the burned surface through the meshes of the tulle grass. The saline packs are replaced every two hours without disturbing the tulle grass. It is essential that dressings should not stick to the raw surface and on no account should wet dressings be left to dry and become adherent. Exquisite pain would then be caused by their removal. The hands or feet are covered with sterile towels and supported at rest in an elevated position. The position of the hands and wrists when at rest is important, the wrist should be slightly dorsiflexed and the fingers kept slightly flexed especially at the metacarpophalangeal joints. The outer dressing, but not the tulle grass, is removed prior to the subsequent baths, the tulle grass floating off in the saline solution. In this way all painful dressings are avoided. Sepsis is prevented and epithelialization in first and second degree burns occurs with surprising rapidity (movement is never lost). In third degree burns, smooth healthy granulations are produced fit to graft in three to four weeks. In some cases epithelial debris separate and form thin white layers over the underlying granulations or newly formed epithelium. The debris should be removed by gentle swabbing during immersion. A bath of soapy water (Lux soap flakes) is useful, or the hands or feet may be given a thorough but gentle cleansing under a light gas and oxygen anaesthetic. The debris appears to be a potent nidus for the development of organisms, hence it is better removed.

51 *Face*—The eyelids and hairy parts are smeared with sterile vaseline and a drop of parolin is instilled into each eye. Under light anaesthesia all loose pieces of skin and burnt debris are swabbed away with pledgets of saline-soaked wool until the surface is considered to be clean. If the burn extends into the scalp the hair should be cut short, well away from the burned area. A gamgee face mask, with an opening for the nose and mouth, is then made to fit the patient. The burns are then covered with sulphonamide powder and tulle grass, and the face mask soaked in saline applied lightly on the surface. Enough jaconet with wool to retain heat and moisture is placed over the dressing, and every quarter of an hour further saline is dripped on the gamgee pad. This may be conveniently done through a drip from an irrigator can, preferably of the thermos flask type, and co-operative patients can often apply

the intermittent irrigation themselves. Fresh gamgee should be applied every 24 hours. Sufficient wool to catch the drips from the pad can be arranged round the neck, or a jaconet collar on a wire hoop, constructed in such a way that it forms a basin into which the overflow runs.

52 Mixed second and third, and third degree burns of the body—When the surface extent of the third degree burn involves wide areas of the trunk or thighs, the method adopted is the continuous flow, constant temperature saline bath, and if the hands and face are also involved these can be treated at the same time. The patient is immersed in a bath of saline. The bath is first filled with thirty-two gallons of warm water, to which is added one gallon of saturated solution of common salt. This gives a 9 per cent. on solution. Water at 105°F, to which is added sufficient salt to form a physiological solution, automatically runs into the bath at the rate of one gallon per minute by means of an automatic device emptying at the head end. A similar quantity of water is allowed to run out from the bottom of the bath by means of an overflow valve. The temperature of the water is controlled by a thermostat. The patient is left in the bath $\frac{1}{2}$ —1 hour, or longer if comfortable. He is then returned to bed and placed on sterile towels under a heated canopy. The bed is wheeled alongside the bath for this purpose. The unburned areas are dried rapidly and the burns powdered with sulphonamide and covered with a single layer of tulle grass, which is in turn overlaid with saline soaked gauze.

53 The normal skin, especially in the neighbourhood of the burn, may become sodden from immersion, but this is uncommon. It can be avoided by reducing the number of baths or interrupting them for a few days. In burns of second and third degree new epithelium growing from the periphery and from scattered central islands appears at the end of the tenth to fourteenth day, and spreads rapidly. In purely third degree burns the sloughs separate rapidly and the raw surface becomes clean and healthy in four to six weeks. The epithelial response is remarkably rapid and progresses steadily. As soon as possible skin grafting by the most suitable method is undertaken. During the whole period movement of the joints is encouraged and stiffening is thereby avoided.

54 The control of infection and the preparation of the raw surface for grafting are matters for skilful and devoted nursing. Efficient treatment is at the same time the best stimulus to epithelization. There is no easy road by antiseptics or dressings occasionally applied and in the full thickness skin losses all efforts must be directed to "conditioning" the surface for the application of grafts. The disappearance of pain is an excellent indication of the control of infection and the correct moment to apply grafts is decidedly by the clinical appearance of the raw surface and the presence or absence of minimal organisms as determined by bacteriological examinations.

Critical Notes and Abstracts

THE BOMBS THE JAPANESE ARE USING

In the air raids on Rangoon and Singapore, the following bombs have been identified —(a) 250 Kg H E bomb, (b) 60 Kg Incendiary bomb, (c) 40-lb Anti-personnel bomb Machine gunning of towns has, in some cases been combined with bombing attack The following details concerning these bombs are offered to our readers —

Incendiary Bombs—Two types are in use, one filled with paraffin wax and another filled with phosphorus pellets On striking the ground, the bombs make a crater of 10 to 26 inches diameter and penetrate to a depth of about 6 feet, depending upon the nature of the ground If the bomb is still "live", the sides of the crater will be clear and smooth, if it has exploded, the sides of the crater will be lined with a grey blue powder caused by the combustion of the chemicals it contained Ignition is indicated by heat and smoke emanating from the crater The *paraffin wax variety* contains a central steel tube filled with thermite It appeared that the composition of the thermite varied at different locations in the tube, the mixture in the centre seeming to contain a higher percentage of iron oxide than the mixture at the tail end The filling is poured in through two filling holes at the tail The whole is initiated by a picric acid charged in the nose of the bomb, detonated by a simple nose pistol The Singapore Fire Brigade advocate water as the most suitable remedy for these bombs The application of water reduces it to what it is—candle grease Ignition temperature of paraffin wax is 473°F and flash point 390°F The *phosphorous type* weighs about 1½ maunds and consists of a filling of a large number of pellets made of rubber or other suitable material of the size of a pigeon's egg, impregnated with phosphorus The length of these bombs from nose to tail is about 3'-6" with a bomb diameter of about 7" The bomb is constructed of $\frac{1}{8}$ sheet iron with a conical nose The nose cap and the exploder which runs down the length of the bomb contain T N T Some of the bombs dropped were dated as far back as 1920 The bomb is fitted with an instantaneous fuse and bursts on impact on a hard surface Many unexploded bombs were found in the soft ground On explosion a high fragmentation is obtained, the splinters from the nose cap and turned collar having a very low trajectory and hence the necessity of taking cover The pellets are scattered wide-spread Some have been located as far as 50 yards from the point of explosion On explosion, the incendiary pellets ignite immediately or within a minute or two, each pellet giving a flame 4" to 6" high and burning at a comparatively low temperature The pellets burn

for 5 to 7 minutes giving off a grey smoke, smelling slightly of burning rubber. As phosphorus oxidises rapidly in air, the pellets set alight to any inflammable matter they come in contact with. A very careful reconnaissance for these pellets will be necessary. As everyone knows who has studied chemistry, phosphorus is kept in water. Water or wet sand are therefore good extinguishing agents, but of course as soon as the water leaves by gravity or by evaporation, the phosphorus would start igniting again. Phosphorus is recognisable by the dense white smoke produced and by the garlic smell. It is essential that any incipient fires should first of all be dealt with by means of the stirrup pump, if the fire has got beyond the control of a stirrup pump, then they should be dealt with large fire-fighting units. The stirrup pump should not be directed on to the phosphorus as this will cause the burning phosphorus to scatter and spread the fire. A Phosphorus Chemist says the best method to extinguish burning phosphorus is to spread wet gunny bags over the fire and then sweep up the wet gunnies into a barrel filled with water, which should be emptied out into a pit. The authorities, however, recommend that the phosphorus pellets should be collected as quickly as possible by means of a metal spoon or any other suitable means, placed in a bucket of water or bucket of wet sand or earth and carried to a place remote from human habitation and free from combustible matter where they can burn themselves out. The pellets should not be touched by hand as they will cause dangerous burns on coming into contact with the skin, nor should they be trodden on as this will spread the trouble. Any burning clothing should be immediately immersed in cold water and carefully examined afterwards for bits of unconsumed phosphorus. Any foodstuffs or liquid contaminated should be thrown away. Phosphorus in the form of a sandwich between thin sheets of celluloid was first used by the British in their attacks on certain Axis forests. This set alight the leaves and vegetation. *Anti-personnel Bombs*—In the early raids on Rangoon on December 23rd and 25th, the Japanese used 40 lb anti-personnel bombs with great effect. The bomb bursts on impact with the ground, forming hardly any crater, just a pot mark, the fragmentation (i.e., pieces or splinters of the bomb casing) following a low trajectory with great lethal effects. Those who took cover in shelter or slit trenches escaped without injury. The Rangoon experience shows that, without any doubt, people are better dispersed in their houses than running out in an attempt to go to trenches or shelter and the policy of "take cover in the house" has been accepted practically everywhere. Buildings in the vicinity of shell burst showed signs of splinter marks on their faces, the main danger extending to an area from ground level to about 8 feet upwards. This demonstrates the importance of obtaining lateral protection behind a well-built blast and splinter resisting wall. Openings in the lower parts of buildings should be protected especially if they are occupied by personnel, apparatus and machinery that must stay there. Taking cover by lying

Critical Notes and Abstracts

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and flying sand or soil, but is not completely proof against penetration by flying steel splinters at 15 feet (the maximum distance at which spray from a stirrup pump can be effectively used on a burning bomb)

- (3) A $\frac{1}{4}$ in ply board, or a dustbin lid, or four thicknesses of folded wet blanket hung in front of the face over one arm gives full protection against molten magnesium and flying sand or soil, but not against steel splinters even at a greater distance than 15 feet

Safety News, March, 1942

THE TREATMENT OF PHOSPHORUS BURNS, POISONING WOUNDS

Treatment—for Burns and Scalds from Phosphorus General Instruction If clothing adheres to the burned surface, do not attempt to remove it, but cut clothing carefully around the burned area

A slight burn may be dressed with sterile gauze covered with butesin picrate ointment, boric ointment, sterile vaseline (petrolatum) or 5 per cent tannic acid Bandage securely but not tightly

A more severe burn should be dressed with sterile gauze covered with butesin picrate, boric ointment or sterile vaseline (petrolatum) The physician can then redress the burn determining its degree and extent

Wash immediately with large quantities of water, then with a 5 per cent solution of sodium bicarbonate Burns should be treated with 1 per cent copper sulphate solution Dress with butesin picrate ointment, boric ointment or sterile vaseline as directed above

Treatment for Phosphorus Poison (Swallowed)

- 1 Induce vomiting by administering the universal antidote — 2 parts pulverised charcoal, 1 part magnesium oxide, 1 part tannic acid

Dose—One heaped teaspoonful in small glass of water

- 2 Administer 2 grms copper sulphate in 100 cc water
- 3 Administer large quantities of water and 5 to 10 cc of oxidised turpentine (turpentine which has had long exposure to air)
Do not give milk or white of egg

- 4 Administer 15 gms of magnesium sulphate in 100 cc water

Authority — "Laboratory Emergency Chart Fischer Scientific Company" As approved by several Public Health Authorities and Administrations in America

Wounds—Wounds caused by yellow phosphorus must be given immediate treatment When a particle of phosphorus comes into contact with the skin, it gives cause to a very severe wound and un-

less the wound is treated immediately, yellow phosphorus enters the blood stream, a much smaller dose may be fatal

Phosphorus wounds should be treated with an oxidising agent such as permanganate of potash or hydrogen peroxide

If the wound is not a deep one and if immediate treatment can be given, a strong liquid of permanganate of potash should be used, the wound being repeatedly washed

In case of deeper wounds or delayed treatment, it is recommended that a 33 per cent strong hydrogen peroxide solution be used. Only after a complete removal of all the yellow phosphorus, and a thorough cleaning up of the wound, can the usual treatment for burns be given

Safety News, March, 1942

PHOSPHORUS AND ITS PROPERTIES

In view of the fact that the Japanese are using incendiary bombs filled with pellets of phosphorus, we offer the following note to those readers who have not had the opportunity to study chemistry. The note will also serve to refresh the memories of those who have

Phosphorus is a non-metallic element and is used commercially, chiefly in the manufacture of matches. It is not found in nature in the pure state. In combination it is widely distributed as phosphates. Calcium phosphate is present in all fertile soils. Bones contain 60% of calcium phosphate to which they owe their rigidity.

The atomic weight of phosphorus is 31 (hydrogen 1). It is denoted by P₄.

Phosphorus is manufactured from bone ash in an electric furnace, calcium carbide being formed as a dangerous waste product. It is generally cast in thin sticks.

Properties—Ordinary phosphorus, also called common, colourless, white (or yellow) is a translucent, almost colourless, waxlike solid. It is soft and can be cut with a knife.

Its specific gravity is 1.8 (water=1). It melts at 44°C and ignites at 30°C.

It is practically insoluble in water. It dissolves in carbon bisulphide.

When exposed to moist air, it undergoes spontaneous oxidation forming dense white fumes. During the process, it phosphoresces or glows, due probably to the formation of ozone. It ignites at 30°C and, since it is practically insoluble in water, it is always kept under water.

The heat of the body is sufficient to ignite it and, therefore, this type of phosphorus must not be handled by bare hands, unless it is under water. Phosphorus fumes are very poisonous, causing rotting of the bones of the jaw and nose.

When dissolved in carbon bisulphide and a few drops are allowed to evaporate, the residual thin stratum of phosphorus is likely to take fire spontaneously, especially in sunlight.

Phosphorus explodes when warmed along with sulphur, and will explode on admixture with carriers of oxygen.

Form of Phosphorus—Phosphorus exists in different allotropic forms, the chief of which are yellow phosphorus and red phosphorus. The red variety is more stable and is not so poisonous. Both forms of phosphorus are used for war purposes. Red phosphorus is generally used for smoke screens, probably because it is non-dangerous to handle but it is also possible to use yellow phosphorus, both varieties giving phosphorus pentoxide when burnt. This is not poisonous, but often other chemicals, generally arsenics, are used to make the smoke poisonous.

The difference in the two varieties is shown in the following tables —

	Red	Yellow
Colour	Chocolate	Colourless
Smell	Tasteless and Odourless	Garlic
Exposure to air	Non-oxidation	Oxidation
Melting point	500—600 C	44 C
Physiological effects	Non-poisonous	Poisonous
Carbon Bisulphide	Non-soluble	Soluble
Ignition Temperature	260 C	30 C Spontaneous
Chlorine Gas	Fires if heated	Combustion

PSYCHOLOGICAL EFFECTS OF AIR-RAIDS

An article on this subject has been contributed by Dr P E Vernon to the October, 1941, issue of the *Journal of Abnormal and Social Psychology*. It is based mainly on the reports of over 50 psychologists and/or doctors, 30 of whom answered a detailed questionnaire. The air-raid experience of these 'informants' appears to have been varied.

The reports suggest that the reactions of most people to an air-raid are similar in all parts of the country, and are influenced chiefly by what previous experiences they have had of raids. Acclimatization even to heavy raids at night is remarkable, though of course there are individual differences. People whose houses have been de-

molished or who have undergone an unusually intense "blitz" very often regress for a time and show less habituation and more nervousness during the next few raids. A reversion occurs also when there is a long spell of immunity from raids.

There is little doubt that being with others helps the majority of people, though again there are exceptions. Some prefer sleep in their own beds under any circumstances rather than the presence of group and activity.

Four main conclusions about mental disorders attributable to raids are drawn from the reports of medical psychologists —

- 1 There have been fewer cases of neurosis than were expected before raids began.
- 2 It is untrue that there have been no cases of mental disorder attributable to raids. In some cases air-raids strain has been a major factor leading to breakdown but in such cases terror or sensations from blast have generally been less important than indirect effects of raids such as extreme fatigue or prolonged dislocation of normal living conditions.
- 3 There have been no new or unexpected types of air-raid neurosis.
- 4 Among persons showing neurotic trends before heavy raids began roughly, one half have shown no change, their existing complaint has pursued a normal course and responded to treatment as usual. Roughly a quarter have become worse and a quarter have materially improved.

EVACUATED CHILDREN AND BOMBED CHILDREN

The October issue of *Mental Health* contains two interesting papers, one mainly on evacuated children the other on impressions of children in a heavily bombed area. The first expresses the view that experience of air-raids and even of actual bombing has caused less emotional disturbance in children, and that evacuation, on the other hand has given rise to more emotional disturbance than was anticipated before war began. This, of course, does not mean that evacuation has not been necessary or advisable.

The second article stresses the need for long time research before generalizations are made, but nevertheless subscribes to the view that children stand up extraordinarily well to a life of disturbed nights and even to extreme emergency such as being bombed out. Tentative figures are quoted indicating that in a group of about eight thousand children, rather over 4 per cent appeared to show signs of strain. Of this 4 per cent 25 per cent were in the age group 11-14 years, 35 per cent in 8-10 year group and 40 per cent in the 5-7 year group. This suggests that the older children, having gained some independence of parental ties, may feel less helpless and also may be more immune from the contagious anxiety of parents.

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ACCIDENTAL INOCULATION WITH SPIROCHÆTA PALLIDA

Clarence Shaw (Archives of Derm and Syph Nov 1941) reports on the accidental injection of *S Pallida* without the dissemination of the organisms or syphilis ensuing

In February 1938 the author accidentally stuck his finger with a needle through a depth of approximately 1/16th inch. The needle was heavily infected with Nichols strain of *S Pallida*, material remaining in the needle showing 8 spirochaeta per oil immersion field. The wound was allowed to bleed freely and 33 per cent mild mercurous chloride ointment was thoroughly rubbed into the finger and hand, and a finger stall filled with mild mercurous chloride was kept over the finger for 10 hours. No other treatment was given. Blood tests (Kolmer, Wassermann and Kahn) before and immediately after the accidental inoculation were negative. X-ray and fluoroscopic examination of the heart showed no abnormalities. Repeated weekly blood tests for 3 months and later repeated three to six monthly tests to the time of reporting the case were negative. The site of injection, skin, mucous membranes and glands were frequently examined for clinical signs. Subsequent X-ray in November 1940 showed no change in heart or aorta. The CSF was not examined. During this entire period there was no clinical or laboratory evidence of syphilis.

He reasonably assumes that despite probable inoculation of *S Pallida*, syphilis did not develop. The author discusses the question of whether the *S pallida* has become attenuated or lost its virulence for man during long residence in the body of the experimental animal and concludes that the bulk of the evidence shows that Nichols strain is capable of infecting man.

In the instance reported here no anti-syphilitic treatment was carried out, or given as prophylaxis. The reason for this was that without a definite diagnosis partial treatment would only confuse the clinical picture. The mercurous chloride was sufficient to kill any spirochaetes locally.

A questionnaire addressed to a number of syphilologists evoked the following answers —

J H Stokes felt that the procedure carried out was a correct one and was averse to giving any form of systematic treatment as prophylaxis. Th Severac stated his belief that a local mercurial antiseptic such as metaphen should be used. He was also against the systematic use of bismuth and arsenic on the grounds that they tended to mask the clinical picture.

J A Kolmer was against the intravenous use of arsenic and bismuth and preferred to keep his subject under observation for at least eight weeks. His reasons concurred with those of others. He had been consulted by twelve physicians who had accidentally pricked their fingers whilst attending patients with acute early syphilis, then blood coming in contact with the injury. In each instance free bleeding was encouraged followed by daily application of 33 per cent mild mercurous chloride ointment for 3 or 4 days. In no instance did infection follow.

Five other syphilologists expressed similar views. On the other hand P J Hanglick thought that mercurous chloride was insufficiently strong, and preferred the use of tincture of iodine as he found it a more powerful antiseptic and possessed of more penetrating powers. He recommended injection of "arsphenamine in case a local lesion is suspected of contamination by the virus."

S W Secker was of the opinion that in the case of possible accidental injection with *S pallida*, 3 injections of arsphenamine should be given in 5 days if the treatment is commenced within 48 hours of possible infection.

J F Mahoney thought that if an arsenical or bismuth injection confused the clinical picture, this was also true in the case of mercurous chloride, as its prophylactic value was dependent on its systematic spirochaeticidal action. Mercury on account of its slow rate of absorption and elimination exerted a protective action over a longer period. As he thought injection was an extremely haphazard procedure dependent both on the preparation and the thoroughness with which it was rubbed in, he preferred the more accurate treatment by bismuth and mercury. Four other syphilologists preferred the use of an arsenical.

Green Baum expressed the view that if the infecting blood was from a patient with chronic syphilis, mercurous chloride treatment was sufficient. But in case the blood came from an acute florid case, he would prefer three doses of arsenic and three of bismuth "spaced as closely as possible."

These and other syphilologists give their opinions on 25 cases in which syphilitic material was supposedly injected. In no case, regardless of whether mild mercurous chloride or arsenic was employed, did syphilis ensue. *S pallida* inoculation may occur without subsequent infection but not in every case. The advantage of using mild mercurous ointment in preference to giving arsenic or bismuth by the parenteral route is that it does not mask the clinical picture in case the patient should subsequently develop syphilis.

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Oldenlandia corymbosa,
Carum Roeletur, Litaneum

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Original Contributions

IRON-REFRACTORY ANAEMIA IN HOOKWORM DISEASE

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The way the severest degree of anæmia in ancylostomiasis improves if inorganic iron is supplied in sufficient quantities, is one of the most impressive experiences in clinical medicine. Increase in erythrocytes and hæmoglobin, in many cases proceeds at a rate of half a million of red blood cells and 10% (Sahli) per week from the second week onwards. The appearance and the behaviour of the patients change to such an extent that one month's treatment usually is sufficient to transform them from waxy pale invalids with features, blurred by œdema, too dull and apathetic to answer questions, to healthy looking, active individuals with excellent appetite, keen on returning to their work which they were unable to perform properly for many months prior to their admission. To maintain this good condition complete deworming has to follow the anti-anæmic course. The fact that this—apparently complete—cure of the anæmia and all its consequences is achieved without any other treatment than iron-medication, especially without infestation was established by Rhoads et al (1934), Napier and Das Gupta (1936-37), and confirmed by Payne and Payne

(1940) and Heilig (1941) This discovery has not become common knowledge and its great practical importance was hardly sufficiently realized By following the rule that not a single dose of the powerful anthelmintics, carbontetrachloride or tetrachlorethylene should be administered to a patient with a hæmoglobin level below 40% (Sahli), all the dangerpoints of hookworm destruction are avoided, whereas to deworm these patients at a lower hæmoglobin value is definitely risky It may be mentioned that every other method of anti-anæmic treatment in ancylostomiasis, except for iron-medication, is useless

Recently a lady, 30 years of age, was admitted to the hospital, she was treated for her anæmia for the last eight years, she had received five hundred (sic!) liver injections (mostly Campolon) and the result was red blood cells 1 33 millions, hæmoglobin 15% (Sahli) The second stool examination, performed after admission to our wards, revealed hookworm ova Subsequently Bland's pills (gr 90 per day), the only remedy given to her, increased the red blood count to 3 25 millions and the hæmoglobin to 40% in three weeks

After seeing a long series of hookworm anæmias responding to anti-anaemic treatment in such a miraculous way, one is all the more surprised to find apparent exceptions to the rule anaemias of exactly the same hypochromic microcytic type, passing hookworm ova in the motion, looking and behaving identically like the others, but not improving on iron, and showing even a slowly deteriorating blood condition To find the cause for this negative response in each of these cases is of the greatest importance and, in fact, the only way to save the life of these patients The following case reports show some of the typical factors, responsible for iron-refractory behaviour in hookworm anaemias

Case 1. Kemp, Hindu ryot of 26 years, admitted 4-9-1941 because of weakness, lassitude, loss of appetite and slight swelling of the legs On examination the patient showed the greyish-yellowish pallor of face, tongue and soft palate as well as the enlarged heart, with all the signs characteristic for ancylostomiasis (Heilig, 1942) Blood pressure 95/40 Tonsils not enlarged, sinuses not tender The respiratory system clinically and radiologically showed no pathological signs Spleen two fingers' breadth below the costal margin Liver just palpable Temperature was normal on admission but it became subfebrile to febrile in irregular intervals of eight to ten

days, the febrile periods lasted for one to three days with temperatures from 99° to 101°, these attacks were followed by completely afebrile periods, no rigor was ever observed. The pulse rate varied from 84–92 during afebrile times to 118 on febrile days.

Laboratory findings on admission: erythrocytes 1.3 millions, hæmoglobin 18% (Sahli), leucocytes 4200, polynuclear 61%, lymphocytes 32%, large monocytes 5%, eosinophils 2%. Malaria parasites absent, malaria flocculation test positive. Sedimentation rate 6/34 (Westergreen). Urine: albumin 0, sugar 0, microscopically nothing abnormal, bacteriologically no growth. Motion: hookworm ova found. Fractional testmeal: free HCl-28, total acidity 8-50.

The treatment initially consisted of Bland's pills, gr 30 tds. The hæmoglobin figures were 24% on 15-9, 20% on 22-9, 17% on 29-9. In spite of seven liver injections (Liverex 5 c.c. daily), added to the iron medication, hæmoglobin was 15% on 6-10. The enlargement of the heart (orthodiagram) and the œdema increased. Meanwhile (30-9) quinine treatment was started with gr 30 daily for seven days and gr 15 for another week. By this time (13-10) the hæmoglobin level was still 15% (Sahli) and the fever chart showed—in spite of a full course of quinine—short febrile periods now and then. The leucocyte count was constantly low, varying between 4000 and 6000, with a moderate lymphocytosis and an increased percentage of large monocytes up to 8%, due to chronic malaria. The hæmoglobin content dropped to 13% (Sahli) on 20-10. The urine culture, showing now (20-10) *Escherichia coli* growing, determined us to give five Pyelopurin injections on consecutive days, on conclusion of this course the temperature rose again to 100° for three days, hæmoglobin 15% on 27-10 and 14% on 13-11, in spite of substituting Fersolate for Bland's pills. The general condition of the patient deteriorated rapidly, the œdema increased. The turning point was reached on 6-11 when the patient reported that he noticed some discharge from the right ear since the previous night. The specialist found an otitis media and treated it accordingly. From now on the hæmoglobin increased rapidly: 18% on 10-11, 26% on 17-11, 30% on 24-11, 35% on 1-12 and 42% on 8-12. Not the slightest rise of temperature was noticed for five weeks after the manifestation of otitis. The œdema disappeared within a fortnight. Deworming with carbontetrachloride (10-12) yielded a moderate number of hookworms—A painless and mostly afebrile otitis media caused the refractory response to iron in a hookworm anaemia.

Case 2. T, a Hindu ryot of 28 years sought admission on 11-9-1941 because of breathlessness on exertion and increasing weakness. He gave a history of fever attacks of short duration, sometimes preceded by a rigor, for the last six years, for the last two months he was afebrile. Examination revealed all the signs of a severe hypochromic anaemia and a heart condition, showing all the characteristic features which are found in hookworm disease, as far

as heart-size,—shape,—sounds,—murmurs and the peculiar expansile pulsation, visualized on radiological examination are concerned. The blood pressure was 100/40 mm Hg. Tonsils and sinuses not infected. Respiratory system normal. Liver enlarged by two fingers' breadth, spleen four fingers' breadth below the costal margin—Within the first fortnight the pulse rate dropped from 110 to 88 and hardly went beyond 90 subsequently. Temperature was subfebrile, hardly reaching 100° the first two days after admission and remained completely normal for the next fifty-two days upto 4-11.

Laboratory findings on admission. Red blood cells 12 millions, hæmoglobin 11% (Sahli). Malaria parasites absent, malaria flocculation test positive. Sedimentation rate 50/100 (Westergreen)—Urine albumin traces, sugar & microscopically erythrocytes ++, leucocytes +, bacteriologically *Escherichia coli*—Motion hookworm ova fairly numerous. Fractional testmeal free HC10-56, total acidity 12-70.

To decide whether hookworm disease, urinary tract infection or chronic malaria were responsible for the severe hypochromic anæmia (hb 11%, colour index 0.49), the patient received only Bland's pills (gr 90 per day) for four weeks—up to 9-10. In eleven days hæmoglobin increased to 16% (Sahli), after one more week to 18%. After four weeks of iron medication (6-10) the values were erythrocytes 12.5 millions, hæmoglobin 18%. The following fortnight one liver injection (Reticulin 2 cc) daily was administered without achieving any improvement of the blood condition (22-10 erythrocytes 14.3 millions, hb 18%). The next five days one Pyelopurin injection was given every day whereas the iron supply was stopped, the hæmoglobin level rose to 21% (Sahli), the urine sediment became normal, culture showed no growth, under renewed iron medication, the hæmoglobin content increased slowly to 26% within the next week (3-11). But in spite of this combined anti-anæmic and urine disinfecting treatment, which took nearly eight weeks to gain 15% (Sahli), the general condition of the patient remained utterly unsatisfying, he still complained of weakness and lack of appetite—Two days later (5-11) a rigor set in and the temperature shot up to 102°, blood, taken at the height of fever, revealed benign tertian rings. A course of five intravenous quinine injections (gr 5 to 10), given on consecutive days, followed by quinine sulph, taken orally for two weeks, changed the clinical picture dramatically. By the end of the intravenous quinine course the hæmoglobin value was 33% and after the second week of anti-malarial treatment it had reached 43% (Sahli). After the administration of carbontetrachloride numerous hookworms were passed and no ova appeared in the motion during the next week. The patient improved during the quinine medication to a surprising extent. For fully four months no malarial attack had occurred and yet, the chronic malarial infection, probably together with a chronic *E. coli* cystitis, prevented the regular response of the hookworm anæmia to iron medication.

Case 3 S, a Hindu clerk of 37 years, was admitted on 20-10-1941 because of breathlessness on walking, weakness and burning sensation on the tongue on taking spicy food. He gave a history of "dysentery" two years ago and of a tendency to sore throat. Examination revealed the usual picture of sallow pallor with waxy conjunctivae, a greyish-white soft palate which showed some slate coloured pigment spots which were visible also on the yellowish white tongue. Specialistic examination showed the tonsils not enlarged, a septum deviation with a spur right ++. The heart was moderately enlarged and a harsh systolic murmur present in the mitral area. Blood pressure 90/50 mm Hg. No pathological signs in the respiratory system. Liver uniformly enlarged, two fingers' breadth below the costal margin, not tender. Spleen not palpable. Temperature was afebrile for irregular periods from two to five days, alternating with subfebrile periods (up to 100°) of one to three days duration. Pulse varied with the temperature between 80 and 110.

Laboratory findings. Red blood cells 1.36 millions, haemoglobin 22% (Sahli), leucocytes 5600, polynuclear 63%, lymphocytes 35%, large monocytes 2%. Wassermann, Kahn and Kline reaction negative. M.F. not found, M.F. negative, van den Bergh indirect +. Sedimentation rate 32/65 (Westergreen). Urine albumin and sugar negative, urobilinogen increased, microscopically leucocytes +, culture no growth. Motion hookworm ova present. Fractional testmeal free HCl, total acidity 8.

Blaud's pills, causing indigestion, were replaced by Fersolate and pepsin-hydrochloric acid was added, apart from this treatment, rice polishing was given (about one ounce per day) in lime juice to increase the intake of vitamin B and C, though the history of a sore tongue pointed more towards a nicotinic acid deficiency. When the haemoglobin level remained constant after two weeks of this medication (3-11 hb 24% Sahli), ten liver injections (Chappel's liver extract, 2 cc) were administered and Cerelexin, "Upjohn", containing the whole B complex, was added. Within this period some erythrocytes appeared and leucocytes slightly increased in the urine, when the culture was repeated, *Proteus* was found. A course of five Pylorurin-injections concluded the second fortnight of treatment, haemoglobin failed to increase (17-11 rbc 138, hb 25% Sahli) and the temperature now remained subfebrile for five consecutive days. Two days later (19-11) temperature, preceded by a rigor, shot up to 102°, malaria parasites were not found but by now the malaria flocculation test had become positive and the spleen palpable. In spite of five intravenous quinine injections (gr v-x) plus quinine sulph gr.x per day orally, the fever continued, assuming an intermittent character, swinging between 97° and 102° every day. On the day of the last quinine injection (23-11) 8000 leucocytes were counted with 73% polynuclear leucocytes, 21% lymphocytes, 5% large monocytes and 1% eosinophils. Haemoglobin 26% (Sahli). Weil-Felix reaction

negative The general condition of the patient seemed to be critical, he was extremely weak, his face puffy, the blood pressure dropped to 80/50 Two days after the conclusion of the unsuccessful anti-malarial treatment (25-11), to achieve disinfection of the urinary tract, Prontosil album "Bayer" medication was started (1 tab tds), within twenty four hours the temperature came down from 103.5°, the highest level ever reached in this case, to normal and remained so for the next fifteen days, up to the date of the patient's discharge (11-12-1941), the whole course of Prontosil treatment with diminishing doses lasted six days and consisted of fourteen tablets The day after its conclusion the hæmoglobin value was 38% (Sahli), the urine was microscopically normal and bacteriologically sterile The intelligent and critical patient felt that his life had been saved By the end of the following week, when only the iron medication was continued, the red blood count was 3.22 millions, hæmoglobin 46% (Sahli) Deworming was performed in the usual way—In this case iron, liver, vitamins, intensive anti-malarial treatment and urine disinfection, attempted with Pyelopurin, failed to prevent a critical deterioration of a hypochromic (hookworm—?) anæmia, which improved splendidly, as soon as a *Proteus* infection was dealt with by Prontosil

Discussion

True or genuine pernicious anaemia is hardly ever seen here and megalocytic (tropical) nutritional anæmia is a rarity, these facts are certainly due to the presence of a good amount of "extrinsic factor" in the food, otherwise the a—or hypochlorhydric gastric juice, which is found in 42% of our hookworm anæmias (Heilig and Visweswar, 1942), could not build from it the "intrinsic factor" in a quantity sufficient to prevent the appearance of megalocytic anaemias in most of these cases A detailed comparison of the diet in North China (Snapper, 1941) or Bombay Presidency (Wills, 1931, Wills and Evans, 1938), where megalocytic anaemias are common, with that used in Mysore, should be helpful in determining the food stuffs which are rich in Castle's extrinsic factor However the problem with which are faced in Mysore in a great number of patients, every day and in ever changing form, is the diagnosis of the aetiology of hypochromic anaemias The temptation is ever present to make the great frequency of hookworm-infestation among our hospital patients responsible for all the afebrile anæmias of this type In the majority of cases the almost immediate response to sufficient doses of inorganic iron, which causes such a rapid and complete improvement of the red blood picture as in hardly any other condition, confirms the

diagnosis of hookworm anaemia Whether an unproved hookworm toxin depresses the function of the bone marrow or the loss of iron with the blood sucked by the hookworms directly causes the anaemia, remains a question open to discussion and further research The fact is that iron medication acts in uncomplicated ancylostomiasis as a specific treatment, even before deworming was performed In many hundreds of such cases we did not find a single exception to this rule, except in terminal stages, so much so that lack of response to iron proves that another infection, co-existent with the hookworm infestation, is responsible for the refractory reaction In our patients, where multi-infection is the rule, it is not sufficient to find out that an old malaria or a urinary tract infection, a middle ear process or a sinusitis or several of them simultaneously are present One has to decide which of these pathological conditions is active, which prevents the improvement or, more often, which causes the deterioration of the anaemia In our experience none of the clinical tests is able to supply a definite clue, the only reliable method in solving these diagnostic difficulties is the therapeutic test By the end of the second week the haemoglobin level of an uncomplicated hookworm anaemia rises by about 10% (Sahli) if iron is supplied in proper doses (Blaud's pills, gr 90 per day), provided that neither vomiting nor diarrhoea interfere with its utilisation Recent investigations (Heilig and Visweswar, 1942) have proved that the effect of inorganic iron is entirely independent of the gastric function, achlorhydric hookworm anaemias responded earlier and more decidedly to iron medication than normo—and hyper-chlorhydric anaemias of the same origin Additional supply of hydrochloric acid does not influence the therapeutic effect of iron, equally useless is the administration of liver extract to such cases If the anaemia is due to hookworm disease iron and nothing but iron is required, if on the other hand the haemoglobin value in a hookworm infested patient has not improved by some 10% (Sahli) and 500,000 red cells after two weeks of iron therapy, the most radical treatment available against any of the accompanying infections has to be started without further delay For practical clinical purposes, when no scientific purpose is at stake, combined treatment should be applied at once, even before the negative response to iron was observed A case, passing hookworm ova, showing an enlarged spleen and/

or a positive malaria flocculation test, leucocytes in the urine sediment, especially when the urine culture is positive, should be treated against all these three infections simultaneously. We use the following therapeutic method along with Blaud's pills, gr 90 per day (orally), quinine bihydrochl gr 5 to gr 10 plus hexamine gr 20 to gr 30, mixed in one syringe, are injected intravenously on five consecutive days. This amount of quinine is sufficient to control most of the malarial infections. If the urine sediment has not substantially improved and the culture shows still some growth, a drug of the sulfonamide group (preferably sulfathiazole) is given, while Blaud's pills are continued and the injections stopped, a course of twenty-one tablets of any of these compounds is our routine dose, almost always sufficient to disinfect the urinary tract.

Conclusion

An anaemia due to hookworm disease improves so quickly and regularly on iron medication without any additional treatment and before deworming is performed, that any delay in achieving this favourable response must be traced to some other active pathological process, co-existent with ancylostomiasis. To determine which of the accompanying infections is responsible for the refractory reaction is of great importance, the only way to prevent further deterioration of the blood condition and thus to save the patient, is to eliminate the one among the usually multiple—pathological conditions which makes the anaemia iron-refractory. In our material, malaria, urinary tract infections, silent middle ear—and sinus-affections usually are responsible for a lack of response to iron in hookworm anaemia. For practical purposes, if no scientific analysis is intended, all the infections present in an individual case, should be treated simultaneously.

Summary

Three cases are reported which show different causes of iron-refractory response in hookworm anaemia.

The difference in the reaction to iron medication is discussed between uncomplicated anaemia in hookworm disease and cases complicated by some other active pathological process.

The diagnostic and prognostic importance of such an iron-refractory reaction is pointed out, the most frequent causes of it are enumerated

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or a positive malaria flocculation test, leucocytes in the urine sediment, especially when the urine culture is positive, should be treated against all these three infections simultaneously. We use the following therapeutic method along with Blaud's pills, gr 90 per day (orally), quinine bihydrochl gr 5 to gr 10 plus hexamine gr 20 to gr 30, mixed in one syringe, are injected intravenously on five consecutive days. This amount of quinine is sufficient to control most of the malarial infections. If the urine sediment has not substantially improved and the culture shows still some growth, a drug of the sulfonamide group (preferably sulfathiazole) is given, while Blaud's pills are continued and the injections stopped, a course of twenty-one tablets of any of these compounds is our routine dose, almost always sufficient to disinfect the urinary tract.

Conclusion

An anaemia due to hookworm disease improves so quickly and regularly on iron medication without any additional treatment and before deworming is performed, that any delay in achieving this favourable response must be traced to some other active pathological process, co-existent with ancylostomiasis. To determine which of the accompanying infections is responsible for the refractory reaction is of great importance, the only way to prevent further deterioration of the blood condition and thus to save the patient, is to eliminate the one among the usually multiple—pathological conditions which makes the anaemia non-refractory. In our material, malaria, urinary tract infections, silent middle ear—and sinus-affections usually are responsible for a lack of response to iron in hookworm anaemia. For practical purposes, if no scientific analysis is intended, all the infections present in an individual case, should be treated simultaneously.

Summary

Three cases are reported which show different causes of iron-refractory response in hookworm anaemia.

The difference in the reaction to iron medication is discussed between uncomplicated anaemia in hookworm disease and cases complicated by some other active pathological process.

pretation of electrocardiograms viz $e_2 = e_1 + e_3$, in which formula a mathematical relationship is expressed between the amplitudes of the deflections in the three leads. In the great majority of electrocardiograms, the validity of Einthoven's formula is proved by finding the deflections in Lead II to approximate in size to the sum of their values in Leads I and III.

Axis Deviation Tracings

On the basis of Einthoven's electrocardiographic studies in cases of valvular disease of the heart, it was claimed for years that axis deviation curves are diagnostic of preponderant hypertrophy of one or other ventricle. In preponderant hypertrophy of the left ventricle, Lead I shows a large R and a small or absent S wave, while Lead III shows a small or absent R wave and a large S wave (Left axis deviation), in other words, the deflections of greatest amplitude in Leads I and III point away from each other or diverge.

In preponderant hypertrophy of the right ventricle, the reverse holds true, in Lead I, R is small or absent and S is large while in Lead III, R is large and S small or absent, the deflections of greatest amplitude in Leads I and III point towards each other or converge.

By weighing the ventricles separately, post-mortem, in cases of valvular disease of the heart, a correspondence between the electrical signs and the weight-ratio of the left and right ventricles, has been established.

Though the above-mentioned electrocardiographic signs are indicative of preponderant hypertrophy of one or other ventricle in the great majority of cases, they should not be considered pathognomonic. Similar tracings have been described by various observers under quite different circumstances —

(1) From alteration in the "lie of the heart" in the chest

Even minor degrees of rotation of the heart on its axis are capable of giving electrocardiographic tracings closely similar to those of preponderant ventricular hypertrophy. Curves resembling those of right ventricular preponderance usually result from rotation of the heart's axis in a clockwise direction,

while anti-clockwise rotation of the heart's axis simulates preponderant hypertrophy of the left ventricle, from the electrocardiographic point of view (Cohn and Reisbeck, Lewis) Much experimental work has been done on this subject by Herrmann & Wilson

In clinical practice, mild degrees of rotation of the heart's axis are common enough The lie of the heart in the chest is subject to influence from various organs, in the neighbourhood During respiration, there is a continuous and cyclic change in the degree of axis deviation of the electrocardiogram During inspiration, there is a tendency towards a dextrocardiogram with large S waves in Lead I and large R waves in Lead III, during expiration, increase in size of the R waves in Lead I and S waves in Lead III suggests a levocardiogram Accumulation of gas in the stomach or intestines, e.g. from carbohydrate dyspepsia, is capable of altering the tracings significantly in the direction of the levocardiogram, in such cases, an erroneous diagnosis of left ventricular hypertrophy is likely to be made As early as 1914, Waller had observed the striking effect of deep respiration on the electrical axis of the heart

According to Master, in most cases of abnormal axis deviation, it is possible to tell from the electrocardiogram which factor (ventricular hypertrophy or rotation of the heart's axis) is operating When left axis deviation results from true ventricular hypertrophy, the QRS complex in Lead III is of high voltage and the S wave in Lead II is prominent, when it results from an alteration in the lie of the heart, then the QRS complex in Lead III is of normal voltage, the S wave in Lead II is not unduly prominent and the P wave in Lead III is frequently inverted

(2) *From disturbances of conduction in the smaller branches or ramifications of the conducting system.* Individual differences in the intraventricular spread of the excitation process are common Alterations in amplitude of the various electrocardiographic deflections have been induced experimentally by Rothberger and Winterberg by dividing the ramifications of the conducting bundles Curves resembling those of ventricular preponderance have been ascribed to damage or disease of intraventricular ramifications of the conducting bundles

(3) It has been suggested by some observers that axis deviation curves may result from dilatation of one or other chamber of the heart, they ascribe this to a lengthening of the path of conduction of the excitation process to the affected ventricle, delay in activation of the ventricle leads to axis deviation curves

Nomenclature

From the above, it will be obvious that left and right axis deviation curves are not necessarily diagnostic of ventricular hypertrophy. For this reason, terms in common use at the present day, such as "left or right ventricular hypertrophy" and "right or left sided preponderance", should be discarded in favour of less committal terms like "left or right axis deviation" and "levo—or dextro-cardiogram". According to Scherf and Boyd, the most convenient term to use in practice is "left or right type of ventricular electrocardiogram".

Of late, American investigators (Wilson and others) have urged a complete revision or rather a reversal in our present-day nomenclature of ventricular electrocardiograms. According to them, tracings which have been labelled levocardiograms in accordance with the classical nomenclature, should be regarded as dextrocardiograms, since they represent earlier activation of the right side of the heart. Much confusion prevails in medical circles as a result of this proposed revolutionary change in the nomenclature of electrocardiograms introduced by the American School of workers. Whether this new terminology will stand the test of time is to be seen.

Methods of Calculating Axis Deviation

Many different methods and formulae have been proposed for determining the electrical axis of the heart. They render it possible for us to judge or classify electrocardiographic records in terms of ventricular preponderance. Methods in use at the present day, for calculation of the electrical axis, are —

(1) Trigonometrical Methods i.e. determination of the angle α or calculation with the use of Einthoven's triangle. For this purpose, a special chart with Einthoven's equilateral triangle is necessary. In order to calculate the electrical axis deviation of a given electrocardiographic record, the heights or amplitudes of the R and S waves are carefully measured in

Leads I and III From this data the values (R_1-S_1) and (R_3-S_3) are calculated, for Leads I and III respectively These values are then charted along the two sides (marked Lead I and Lead III) of Einthoven's triangle From these two points perpendiculars are dropped towards the centre A line is drawn from the centre of the triangle and through the point of intersection of the two perpendiculars to meet the circumference of the circle embracing Einthoven's triangle The angle of deviation is read off at the point at which this line cuts the circumference of the circle

Normal electrical axis is said to be between 0° and $+90^\circ$ of the circle Minus values suggest left axis deviation while plus values greater than 90° suggest right axis deviation

(2) The "simple" or "clinical method" For this purpose, a simple formula is employed —

"Index of axis deviation" (R_1+S_3) — (R_3+S_1) where R_1 and R_3 represent the amplitudes of R in Leads I and III and S_1 and S_3 represent the size of S in Leads I and III respectively

The sum of the amplitudes of R_3 and S_1 when subtracted from the sum of the amplitudes of R_1 and S_3 gives the index of axis deviation An index greater than $+30$ indicates abnormal left axis deviation, with a wide borderline of $+20$ to $+30$, values under -15 indicate right axis deviation, with a borderline of -10 to -15 (Paul White) Though values falling within the borderline zones of $+20$ to $+30$ and -10 to -15 have been regarded as falling within the limits of normal, it is perhaps more correct to regard them as examples of mild axis deviation

Other formulae have been suggested and employed for calculating the index of axis deviation e.g

(A) Index = ($R_1 - R_3$) + ($S_3 - S_1$) proposed by Lewis

(B) Index = ($U_1 + D_3$) — ($D_1 + U_3$) where U is the height of the largest upward deflection of QRS and D is the height of the largest downward deflection, the numbers indicate the leads used This formula was proposed by Paul White

The Present Study

Object of study — This investigation forms part of a study of normal electrocardiographic records of Indian subjects, un-

dertaken with the aid of a medical research grant from the Trustees of the late Sir Ratan Tata. An analysis of the various "deflections" and "intervals" of the normal electrocardiogram has already appeared in print.

This paper deals with the electrical axis deviation of normal Indian School-children. Though the subject of axis deviation has been investigated in the past by various workers, their work does not apply to Indian subjects.

Selection of Material The present paper deals with fifty normal electrocardiograms selected at random from well over one hundred and fifty normal records of children of school-age (5-15) yrs. Twenty five records were of school-boys and twenty five of school-girls. Students were selected for this study with great care, students with any suggestion of weakness or disease of the heart or other organs were rigidly excluded. The electrical axis deviations were determined in these cases by means of Einthoven's triangle and the "index of deviation formula".

Results of Investigation

Axis Deviation by the Trigonometrical method

The R and S waves were measured in Leads I and III in each of the fifty records. In some records, phasic variations in the amplitudes of the R and S waves were evident on account of respiratory movements of the chest. In such records, the average value of R or S was calculated for each lead, by adding the maximum and minimum values of the deflection in the

Table I

Values of axis deviation in fifty normal children calculated with the aid of Einthoven's triangle

Boys (aged 5 to 15)				Girls (aged 5 to 15)			
Case Number	Angle of Deviation	Case Number	Angle of Deviation	Case Number	Angle of Deviation	Case Number	Angle of Deviation
1	+45°	15	+7°	1	+12°	15	-29°
2	+6°	16	+90°	2	+25°	16	+45°
3	+8°	17	+39°	3	+71°	17	+31°
4	-35°	18	+45°	4	+73	18	+14°
5	+3°	19	+80°	5	-54°	19	+107°
6	+49°	20	+75°	6	+83°	20	+105°
7	+61°	21	+53°	7	+67°	21	+65°
8	-31°	22	-44°	8	+74°	22	+38°
9	-53°	23	+54°	9	+6°	23	+64°
10	-82°	24	+4°	10	+77°	24	+71°
11	+23°	25	+9°	11	+51°	25	+77°
12	-42°			12	+4°		
13	-54°			13	+16°		
14	+75°			14	-7°		

lead and dividing by 2. For example, if the R wave amplitude in Lead I of a given record shows respiratory variations and shows minimum and maximum values of 7mm and 10 mm respectively, then the average value of R for that lead is taken as $\frac{7+10}{2} = 8.5$ mm. On the whole, this method of calculation was found to be the most convenient method of minimizing errors due to the phases of respiration.

Having calculated the R , S_1 , R and S_3 values of each record, the angle of electrical axis deviation was calculated for each electrocardiographic record with the use of Einthoven's triangle, as described in an earlier paragraph. In table I, we reproduce an analysis of the angles of axis deviation in the present series of fifty normal records from school-children.

The mean value for the angle of axis deviation or angle alpha, taking all cases into consideration, was $55^\circ 5$.

In the series of normal electrocardiograms from female students, recently reported by Hoskin and Jonescu, the mean value for angle alpha was $+54^\circ 5$. While my series deals with children of school-age, that of Hoskin and Jonescu deals with young adults. In spite of this disparity in age groups, the final value of angle alpha is closely similar in the two series of cases.

In three records of the present series there was abnormal right axis deviation by the trigonometrical method, the values of angle alpha in these three cases being $+105^\circ$, $+107^\circ$ and $+127^\circ$. Clinically, the hearts of these children were pronounced as perfectly normal. Four records showed abnormal left axis deviation, the values of angle alpha being -7° , -29° , -35° and -44° respectively, clinically, these children were perfectly normal. 14% of our cases showed abnormal axis deviations. Hoskin and Jonescu found abnormal deviations in only 6% of their cases. (For further details about the angle of axis deviation, see Table II).

Sex differences. The average value of angle alpha for the whole series was $55^\circ 5$, for male subjects it was $54^\circ 6$ and for female subjects $56^\circ 5$.

In boys, the value of angle alpha ranged from -44° to $+90^{\circ}$, there being two records showing abnormal left axis deviation, abnormal right axis deviation was not observed in a single instance. In girls, the value of angle alpha varied from -29° to $+127^{\circ}$, there being two records with abnormal left axis deviation and three records with abnormal right axis deviation.

Distribution of records with regard to angle alpha. This is clearly shown in Table II. The angle of axis deviation was found to lie between $+37^{\circ}$ and $+54^{\circ}$ (a range of 18 degrees) in as many as 32% of records.

In no record, was the angle found to lie between the values $+55^{\circ}$ and $+63^{\circ}$.

Table II

An analysis of the angle alpha in 50 records (Percentages)

Angle of Axis Deviation (Range in degrees)	Type of Deviation	No. of records	Percentage of Total
-45° to 0	Left axis deviation	4	8%
-5 to 10°		1	2%
10 to 20°		3	6%
20 to 30°		2	4%
30 to 40	Normal range of Electrical Axis Deviation	5	10%
40 to 50		6	12%
50 to 60		7	14%
60 to 70		6	12%
70 to 80		9	18%
80° to 90°		4	8%
90 to 135°	Right Axis Deviation	3	6%

Table III

The index of axis deviation in 50 cases

	Index of deviation (Range)	No. of cases	Percentage frequency
Right axis deviation	-20 to -15	2	4
Borderline cases	-15 to -10	2	4
	-5 to 0	5	10
Normal axis deviation	-5 to 0	14	28
	0 to 5	11	22
	5 to 10	12	24
	10 to 15	1	6
	15 to 20	1	2
Borderline cases	20 to 25	0	0
	25 to 30	0	0
Left axis deviation	30 and over	0	0

Iris Deviation by the "simple" or "formula method"

The "index of axis deviation" was calculated in each of my fifty cases according to the following formula —

$$\text{Index} = (R_1 + S_2) - (R_3 + S_1)$$

Case Reports

AN UNUSUAL CASE OF RAT-BITE FEVER

By

RUSTOM JALVAKIL

M D, (I O N D), M R C I (I O N D), D T M & H, F R F P S G, J P

^{AND}
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M B B S,

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Our purpose in this case-report is to record an unusual type of Rat-bite fever case, with multiple "gummatous" lumps in the muscles and periosteum, which showed immediate response to arsenical therapy

A Muslim male, aged 40, was admitted to the K E M Hospital, Bombay, on 13th December, 1941 for fever and severe pains in the muscles and joints of the body. There was a definite history of rat-bite on the left leg, about four weeks before admission. Soon after the bite he had developed severe oedema of the left leg, intense pains all over the body, mental depression and high fever. He was given two injections of Sulfarsenol which set him right within a couple of days, the oedema, fever and pains had disappeared completely and he was back at his work. After an interval of three weeks there was a sudden return of all his symptoms, viz fever, oedema, muscle-and joint-pains, he complained of lassitude and of local areas of tenderness in the limbs. On examination, he was found to have (1) a spherical lump almost 3 inches in diameter over the anterior aspect of the left thigh. It was tender to touch, fixed to the deeper tissues but not to the skin or subcutaneous tissues, fairly hard in consistency and with a smooth surface. (2) A tender lump in the left anterior axillary fold, about 1½ inches in diameter, it appeared to be within the bulk of the left pectoralis major muscle. (3) A small lump about 1 inch in diameter in the muscles of the right arm. There was no enlargement of spleen or lymph-nodes. The Kahn Reaction of blood was "two plus". The white cell count was 10,000 per cmm, with 72% polymorphs, 20% lymphocytes and 8% mononuclears. The average temp was 102°F. After two injections of Sulfarsenol (intramuscular), 12 and 18 ctg respectively, all symptoms disappeared within thirty hours, including the lumps. When discharged from hospital on the 29th, December, 1941, the patient was in perfect health, except for a small residual lump, ½ inch in diameter, over the anterior aspect of the left thigh.

Three weeks after discharge from hospital, the patient had another attack of fever with severe muscle-and nerve-pains and asthenia, this also responded immediately to an injection of 18 ctg

of Sulfarsenol Since that time, the patient has had two further attacks of a similar nature at intervals of three weeks, each responding immediately to one single injection of 18 ctg of Sulfarsenol Altogether, the patient has therefore had five attacks of fever, asthenia and pains in the muscles and nerves, subsequent to the rat-bite The interval between attacks has been three weeks throughout the course of his illness

Comment

In view of the definite history of rat-bite prior to the illness, the dramatic therapeutic response to small doses of Sulfarsenol and the characteristic clinical picture (fever, asthenia and muscle-pains), one is justified in regarding this case as one of Sodoku or Rat-Bite Fever There are two features in this case sufficiently unusual to warrant comment (1) The development of painful and tender "gummatous lumps" in the muscles of the right arm, the left thigh and the left axillary fold, during the second attack of fever In the extensive literature on Rat-bite fever, there are frequent references to cutaneous manifestations, e.g macular or urticarial lesions Painful, subcutaneous lumps have also been described

"L'exanthème peut être remplacé par des papules de la dimension d'une lentille ou d'une pièce de 2 francs, enfin par un semis de nodules sous-cutanés très douloureux, gros comme des amandes" (From "Maladies Infectieuses et Parasitaires, tome I, Paris 1924)

I can, however, find no reference in the literature to the occurrence of large and painful intra-muscular lumps, as observed in this case

(2) The persistent nature of the infection in the present case is exceptional, there were as many as five distinct attacks of fever with asthenia and muscle-pains, with intervals of three weeks between attacks The usual course of events in cases of Rat-bite fever is to get complete and lasting recovery after the first attack, provided arsenical treatment is given

Summary

An unusually persistent case of Sodoku or Rat-bite fever is described with peculiar, multiple, intra-muscular, gummatous lesions,

Note

Since writing this paper, we have searched through the files of the K E M Hospital Bombay, extending over a period of five years, for cases of Rat-bite fever of the type described above We can find only one case of a Hindoo male aged 40, admitted to hospital in August, 1937, who besides having fever, asthenia and diarrhoea after a rat-bite on the right forearm, also had lumps or swellings described in the left leg and in the right forearm, these lumps disappeared within a few days after the commencement of Sulfarsenol therapy

Analytical Review

PREVENTION OF DIABETES MELLITUS

By

C C MERCHANT

M B S

(from the Pharmacological Dept, Seth G S Med College, Bombay)

(Continued from p 293)

PREVENTION OF DIABETES AND ITS COMPLICATIONS

The problems relating to prophylaxis and treatment being similar in aim and nature may be considered together and under the following heads —

(1) Those relating to prevention of hereditary transmission of Diabetes

(2) Those relating to prevention of diabetes among persons who may be considered as potential Diabetics by reason of (i) history of diabetes in their near blood relatives (ii) they being obese or showing a tendency to do so or (iii) existing liver or gall bladder disease or (iv) disease of some endocrine gland, e.g., acromegaly, Grave's disease etc.,

(3) Those relating to detection and treatment of latent or very mild cases of diabetes with a view to prevent them from drifting into well-marked clinical conditions

(4) Those relating to prevention and early detection of diabetic complications

(5) Those relating to treatment of diabetic women during pregnancy

(6) Those relating to treatment of diabetic children and the aged

(1) *Heredity* — Prevention of hereditary transmission of diabetes

‘Two diabetics should not marry and have children’

Under the present state of our knowledge the only way possible to eliminate diabetes from the community is to stamp out the families which carry the disease as an hereditary characteristic. This can be achieved in two ways (1) By not allowing marriages except between two persons who are themselves non-diabetics and have no

diabetic family history (i.e. non-carriers) This is for all practical purposes impossible as long as boys and girls ignorant of these principles of nature will continue to be attracted and fall into love with each other, and also because it would be rather hard to obtain true family history of persons intending to join in matrimony But in any case, it is most inadvisable in the interest of the future generation to allow marriages between two known diabetics, or between persons whose very near relatives have been known to be diabetics

(2) By preventing children from being born to diabetic parents either by the use of ordinary modern contraceptive methods or by sterilizing one of the partners, but particularly the wife if she happens to be diabetic Diabetes involves no danger to man but because of parturition, a diabetic woman is exposed to much danger

Both contraceptive and sterilization methods should be regarded as very difficult to be put into practice According to the known law governing the transmission of diabetes, nearly one fourth of the population of the world may be considered to be diabetic To expect so many people to practise contraception is just to live in fool's paradise On the other hand, sterilization on such a large scale cannot be carried out without creating a great commotion and furious opposition from the community Further, we do not know yet of any method which would enable us to recognize carriers from amongst—brothers and sisters of a diabetic family

The problem of heredity requires further investigations and study before any practical scheme of preventing diabetes by eugenic methods can be formulated In the meantime, however, the warning given by Joslin to diabetics should be given a serious thought and consideration "Be careful, diabetics, with whom you fall in love"

Marriage of a diabetic?

Joslin in answering the query "shall a diabetic marry", says that 'No diabetic girl or boy should marry (1) unless the other party is non-diabetic, (2) unless the parents of the non-diabetic have been told that the other party is diabetic, (3) unless sufficient capital is available to provide for a sick fund in case of emergency or pregnancy (4) unless there is proved good health apart from diabetes, (5) unless the contracting parties have known each other long enough to realize what the treatment of diabetes by diet and Insulin involves, (6) unless the two have such strength of character that they are prepared to sustain the shocks of life with smile, (7) unless a diabetic is sensible and follows the general line of treatment

(2) Prevention of diabetes among persons who may be considered as "potential diabetics"

(1) *Family History* —Here the diabetic parents should strive to protect the children by taking extreme care as regards diet and exercise, and to prevent them from becoming obese The urine

or such children should always be examined for sugar very frequently. Grown up persons with a hereditary tendency should always try to keep their weight a few pounds below normal for their height, age and built, specially after the age of 30-35 years, the period when diabetes is most likely to develop. Their diet should be frugal consisting of simple food, simply prepared. It should not contain rich highly seasoned dishes, and its caloric value must be just sufficient to maintain a normal or slightly subnormal body weight—which is a great insurance against diabetes. Persons predisposed to diabetes should take plenty of exercise as the latter promotes greater utilization of carbohydrates. Mental workers should have occasional vacation and frequent periods of relaxation, whilst persons of an excitable nature should try to cultivate coolness and equanimity of mind. Such persons should submit themselves to frequent medical examinations, including sugar and blood tests at least once a year, and should seek medical advice without delay at the earliest sign of diabetes.

Joslin's advice to such persons is—"Do not become forty and fat", and if you are a diabetic put this same rule in force amongst your relatives and teach your descendents to avoid obesity." By such means much of the elements of heredity can probably be overcome.

(11) *Obesity* —Joslin "To inherit diabetes is blameless, to acquire it through obesity plus heredity is blamable."

Obesity of any type is a fore-runner of diabetes especially in persons with a family history, and must always be prevented. It has been definitely known that diabetes develops at an age between 11 and 13 in tall and overgrown children and in adults mostly between 45 and 55 years, and that slightly underweight individuals are less liable to become diabetic than those above standard weight. This latter fact should serve as a good warning and eye-opener to obese persons specially if they happen to be relatives of a diabetic. Obesity just like diabetes is considered to be an hereditary disorder and therefore all precautions should be taken to prevent obesity in children of stout or obese persons. Great attention must be paid by the members of a diabetic family to avoid obesity and better to keep their weight 5 to 10% below the standard weight at any time of their life, but more particularly after 30 to 35 years.

Whatever the type of obesity may be, the food must be restricted so that its caloric value at first is slightly lower than that of the output in order to utilize the body fat. Under no circumstances the caloric intake should exceed that of output. Reduction of weight is carried out by a diet equivalent to 1200-1400 calories, containing proportionately less fat and carbohydrate as to avoid fat formation and by stimulating metabolism by giving a relatively larger amount of protein and by increased exercise. If these measures fail, then

thyroid and other glandular preparations may carefully be tried, and their effects watched

In actual practice, the diet is made up of lean meat, fruits, and green vegetables with only enough sugar, starch and fat to prevent feelings of hunger and weakness. In putting patients on such a diet it is wise to make a slow and gradual change till the diet is found which produces a steady fall in weight. This diet is adhered to, till the desired reduction in weight is produced. In the beginning, exercise must be carefully graduated and designed to improve breathing and posture.

During recovery from acute illness patients often show a great tendency to become stout, and if no precautionary measures are taken may weigh much more than before the illness. Such a tendency to stoutness should be recognized, and promptly checked.

(iii) *Liver and Gall Bladder Diseases* — Use of mineral waters

All affections of the liver and gall bladder must be carefully and promptly treated. Gall stones are known to usually precede diabetes and may precipitate it by direct extension of infection to the head of the pancreas than to the rest of it. Hence all cases of gall stones as well as cholecystitis should be operated upon with the removal of gall bladder. Liver plays an important role in carbohydrate metabolism and therefore the activity of its cells must be carefully preserved by medicinal and dietetic measures. Patients suffering from frequent attacks of biliousness or from catarrhal jaundice should be treated with care and be given plenty of carbohydrates in the form of glucose and Insulin to protect the liver cells against further injury. Protein and specially fat are to be much restricted.

Mineral waters such as Vichy, Carlsbad, Marienbad and saline purgatives have been found to have a favourable influence on liver, and also in diabetes. It has been established by exact studies that mineral waters containing sulphate of soda reduce the contents of sugar in the blood of patients after fasting (Roubitschek—Arnoldi), augment the alkali reserves and improve the utilization of the carbohydrates (Kaufmann-Costa and R. Zorkendorfer). In animal experiments, even an increase of glycogen in the liver was found (Arnoldi). The sulphate of soda pharmacologically is said to have a stimulant action on the liver cells. Probably it also influences the assimilating function of the liver, especially the formation and fixation of glycogen, an assumption supported by animal experiments (Diabetic Jour Vol I, No 10 P 27, 4-37).

(iv) *Endocrine Disorders*— In persons showing a tendency of pituitary hyper-activity (acromegaly), pituitary gland may be exposed to Roentgen rays. How far the treatment will succeed is very difficult to say, but in suitable cases a trial should be given. Cases

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disease, the objects of treatment and to recognize and report the changes either for the better or worse under any particular treatment. To this end, he should be educated in the technique of urine examination (tests for sugar and acetone bodies), in elementary principles of dietetics and in computing food values, in self administration of Insulin and in the signs of oncoming trouble specially hypoglycaemia and acidosis and in the use of emergency measures. A diabetic should be made to appreciate the fact that his fate may depend upon his understanding of the disease and his conscientious co-operation with his doctor together with his willingness to play the game according to the rules. Gross violation of the rules may mean serious complications or even death.

Hospitalization

In the beginning, the diabetic patient should be watched closely and treatment should better be carried out in a hospital or a nursing home for at least 2 or 3 weeks during which period clinical investigations, education and discipline may all be carried out. If the case is severe, the patient should however remain for a longer time in the hospital. The diet of the patient should be varied from day to day so that he may learn about substitutes. He must also be taught how to adopt his life to his new condition and how to arrange his diet to suit his work, pocket, and taste. After discharge from the hospital the patient should continue to examine his urine at home at least twice or thrice a week or even daily for sugar and acetone bodies, and the findings reported to his medical adviser whom he should visit at frequent intervals, especially in the beginning. As the condition of the patient improves and his maintenance diet firmly fixed, so as to keep his urine sugar-free for most of the day, he may slightly relax his vigilance. Blood-sugar estimations, though of value, can easily be dispensed within the routine management of the case, but should be made when glycosuria is not brought under control and acetone bodies appear in the urine in spite of active treatment or when attacks of hypoglycaemia frequently occur.

Fundamentals of diabetic treatment D I E

Three letters DIE representing Diet, Insulin, and Exercise are very important in the life history of the diabetic. They are the three mainstays for the health, happiness and long life of the diabetic, when acting alone they are useless or even may prove dangerous, but when well-balanced with each other, they bring about complete utilization of carbohydrate in the diet and render the patient almost normal and symptomless.

The chief aims in the treatment of an uncomplicated case of diabetes should be always (1) to keep the urine sugar-free for most part of the day, (2) to maintain blood sugar at a normal level or

little if any, above normal, (3) to maintain body weight and strength for ordinary physical and mental work

DIET —Fundamental Concepts about diet in the treatment of Diabetes Mellitus

In spite of Insulin at our disposal, diabetic management still remains the back-bone of diabetic treatment, though Insulin has almost done away with the painful starvation to which diabetics of pre-insulin days were subjected. Overnutrition is to day just as harmful for the diabetics as it was in the pre-insulin era. The use of unlimited diet with massive doses of Insulin is to be as much deprecated if not more, as starving the patient with little or no Insulin. The aim of the present day treatment of diabetes is to maintain the patient at a weight which is normal or better 5 to 10% below normal, for the height, age and built of the patient, with or without the use of Insulin, the latter is indicated when the diet suitable for the needs of the patient alone will not control glycosuria.

Requirements of the diabetic diet

Successful treatment of diabetes depends upon the carefully planned diet which should essentially satisfy a few requirements (1) The diet must contain sufficient calories which would maintain weight at a normal or slightly below normal level (2) Protein allowance though comparatively low, must be more than enough to maintain nitrogenous equilibrium (3) Fats must be low enough to avoid ketosis, lastly (4) Carbohydrates must be sufficiently restricted as to prevent them from being wasted through urine.

Caloric value of the Diabetic Diet

Caloric needs

The average caloric requirements of a normal adult male weighing about 150 lbs (i.e. 75 kilo) and doing moderate work is calculated between 3,000 to 4,000 calories per day. It is stated that the basal metabolic rate of an average Indian adult is about 10% less and therefore his caloric requirement is less than that of an average European. An average well-balanced diet contains the essential principles carbohydrate, protein, and fat in the ratio 3 to 4 1 1 with a total 300-400 gms carbohydrate and 100 gms each of protein and fat and it yields about 2,999 calories. The vegetarian diet of an average Indian is rather poor in protein though its caloric value is about equal to that of a mixed diet. Most of us are used to and like a high carbohydrate diet which is also comparatively cheap.

Under nutrition

The basal metabolic rate of diabetic is known to be below normal being about 0.7 instead of 1 and he does much better on a diet of comparatively low basal caloric value (about 1200 to 1500). However the total caloric requirement of a diabetic, like that of a normal person, varies with the age, sex, weight, height, body surface, physical activity, state of nutrition, and many other factors. Whilst planning the diet of a diabetic, all these factors require to be con-

sidered It has been shown that diabetes runs a comparatively mild course and is better controlled when metabolism is kept somewhat below normal by maintaining the weight at a level slightly below normal (10%) During the days just before Insulin was discovered the principle of under-nutrition was regarded very important in the treatment of diabetes and formed the basis on which Allen's method of treatment of diabetes depended The years 1914-1921 are usually referred to as Allen era

Wilder (1922) found that the ability of a diabetic to utilize glucose varies inversely with the metabolic rate and when the rate was lowest, the glucose utilization was best and acidosis was better controlled For this reason the diet of the diabetic patient must be low but must permit enough food, just to meet his maximal requirements without his drawing on his body tissues In case of overweight persons who form a great majority of diabetic patients, the weight should be just brought down to normal or below normal by greatly reducing the caloric value of the diet For a diabetic doing moderate work, a diet approximately containing 1700-2000 calories divided into 200 gm carbohydrate, 70 gm protein, 100 gm fat, is at present recommended by a majority of experts Such a diet closely approximates the normal one, and has proved most satisfactory

Joslin's basic diabetic diet (1937) contains 1600 calories divided between carbohydrate 150 gm ($\times 4 = 600$ cal), protein 70 gm ($\times 4 = 280$ cal) and fat 80 gm ($\times 9 = 720$ cal) *
Carbohydrate allowance —

It must be remembered that 100% of carbohydrate, 58% of the protein, and 10% of the fat eaten as food can be metabolized into glucose Thus the total potential sugar content of a normal diet such as given above would be

400 gm of carbohydrate = 400 gm glucose
58% of 100 gm of protein = 58 gm „
10% of 100 gm of fat = 10 gm „

Total 468 gm glucose

* A BASIC DIABETIC DIET						
Food		Portions	Weight grains	Carbohydrate 150 gm	Protein, 70 gm	Fat, 80 gm
				Cal 1600		
				C, P, F		
				Total Gms		
				C	P	F
Bread	3 slices each	30	(C 18 P 3) $\times 3$	54	9	0
Oatmeal	1 large saucer	30	(drv) C 20 P 5 F 2	20	5	2
Orange	3 Medium each	150	C 15 $\times 3$	45	0	0
5 per cent vegetables	4 portion each	150	(C, 5 P 2.5) $\times 4$	20	10	0
Milk	$\frac{1}{2}$ pint	120	(C 6 P 4 F 4)	10	8	28
(cream 20 per cent	$\frac{1}{2}$ pint	120	(C 4 P 4 F 24)			
1 egg	1		P 6 F 6	6	6	6
Meat	2 small each	60	(P 16 F 10) $\times 2$	0	32	20
Butter	3 pats, each	10	F 8 $\times 3$	0	0	25
				149	70	81
				or		
				150	70	80
				$\times 4$	$\times 4$	$\times 9$
				Calories = 1600		
				600 280 720		

(From Joslin, The Treatment of Diabetes Mellitus 1937)

On such a diet, a complete diabetic whose sugar tolerance is nil might be expected to pass in his urine each day nearly 460 gm of sugar but in practice such amounts in urine are never found. The amount of sugar in the urine will however tell us of the severity of the disease, 100 gm of glucose in the urine will mean a moderately severe, whilst 10-15 gm per day of glucose in the urine would be considered a very mild case of diabetes.

The tissues of a diabetic because of insufficiency of Insulin cannot utilize to the fullest extent the principal source of calories in the food i.e. carbohydrate. The chief problem in the treatment of diabetes is therefore to provide only such amounts of carbohydrate as can satisfactorily be oxidized in the body — without any being wasted in the urine, and as would prevent the patient from being actually starved. Carbohydrates in the diet with the additional sugar which may be derived from protein and fat should be sufficient to make up a fairly palatable and adequate diet. But in case, the sugar tolerance is so low that a fairly sufficient amount of carbohydrate cannot be given to make up the required calories and to render the diet palatable, without producing glycosuria Insulin must be administered.

In pre-insulin days, the type of diet advocated was characterized by its low carbohydrate content. In order to make up the caloric deficit caused by restricted carbohydrate, fat which yields weight for weight more than double the number of calories as carbohydrate and protein, was allowed in liberal quantity. The ratio of carbohydrate to fat in such diets, was the reverse of that present in ordinary diets, and although the dangers of such diets might have been well-known, still there was no means available whereby carbohydrate utilization could be increased.

The present day method of treating diabetics on the principle of undernutrition and pancreatic rest, may be said to have originated since the time of Allen. In 1913, he emphasized the evils of high fat feeding and pointed out the value of undernutrition. Similarly Guelpa in 1910 and Graham (1917) had referred to the value of undernutrition in the treatment of diabetes. In 1912, Schaffer and Woodyatt and others pointed out that the amount of fat in the diet which may safely be given without predisposing to ketosis was limited by the amount of available sugar in the diet (*ketogenic-antiketogenic ratio*). Then came the epoch making discovery of Insulin in 1922. Insulin has made possible the greater utilization of carbohydrate and to increase its amount in the diet, which in its turn has permitted to take diet of an adequate caloric value with more fat and without danger of producing acidosis.

High Carbohydrate diet

Very early, even before Insulin was discovered, Joslin had made the following observations —(1) that in those countries where the

diet is largely carbohydrate the diabetes is mild, (1) in India) (2) that the diets of those diabetics who live longer, whether they show sugar or not are those whose carbohydrate has never been long reduced to a very low quantity, (3) that it is more rational to tend towards than to deviate from the standard diet of healthy people, and lastly (4) that a diet low in carbohydrate but high in protein and fat causes hyperglycaemia and lower, at least temporarily, the tolerance for carbohydrate

In accordance with these observations, there has been a gradual increase in the carbohydrate allowance of the diet used in Joslin's clinic since 1915 when 26 gm per day was the average as contrasted with 100 to 160 gm in 1930, and in upper daily limit of 200 gm in 1935

Since the discovery of Insulin, as a result of a large number of clinical as well as experimental observations, diets with carbohydrate in relatively large amounts have been advocated and prescribed in a great number of diabetic clinics. Amongst those who have studied and advocated the use of new liberal carbohydrate diet may be mentioned the names of Geyelin (1926-35), Sanson (1926-33) and his associates, Adlersberg (1929-32), Poulton (1931), Rabinowitch (1930-35), Dyke (1932), Graham et al (1932), Klemmer (1932), Nixon (1932), Himsworth (1931-34), Barach (1930-37), Peck, and Richardson (1936)

Though all are agreed upon the importance of relatively large amount of carbohydrate in the diet, there are many schools of thought as regards the actual quantity of carbohydrate to be allowed in a diet with regard to its protein and fat contents. The type of diet as favoured by Joslin, Von Noorden, Lawrence and many others, contains carbohydrate ranging from 120 to 125 gm but the fat has been reduced to an average of 90 to 100 gms. The total caloric value of such a diet usually does not exceed 1600 calories (25-30 calories per kilo body weight), in accordance with the well recognized principle of undernutrition. Such a type of diet has been found more palatable and pleasing to the patient, besides making the patient less conscious of his diabetic condition.

On the other hand, others including Rabinowitch, and Richardson recommend a diet which contains on an average 200 to 300 gms of carbohydrate, still keeping the caloric value of the diet to 25 calories per kilo body weight, by greatly reducing fat to 40 to 50 gms in the diet (about $\frac{2}{3}$ to 1 gm per kilo body weight)

It was feared that by increasing greatly the amount of carbohydrate in the diet, there would be an increased quantity of Insulin needed to control glycosuria, but it has been amply shown that this is far from being the case (Sweeny J S 1927, Himsworth 1934), and that on the other hand a diet (eg Barach's) high in carbohydrate results in an increase in sugar tolerance (J.A.M.A 9-4-32)

9 calories per gm in contrast to 4 of protein, (2) the specific dynamic action of fat is lower than that of protein, which would therefore not much increase metabolism, and (3) only 10% of fat is converted into sugar. But it suffers from one serious disadvantage is that it requires carbohydrate for its proper utilization, 1 gm of fatty acid requiring about 1 gm of carbohydrate. When this amount of carbohydrate is not available, fat is incompletely oxidized and there is a danger of acidosis being produced. Hence the amount of fat which can be given in any diet is restricted and kept within the figure permitted by the ketogenic-antiketogenic ratio—($F = 2C + \frac{1}{2}P$) formulated by Woodyat and Schaffer. Woodyat later found that this ratio did not hold good under all conditions and required modification. It was noted that (1) patients kept on a diet in strict accordance with this ratio ran the danger of ketosis, (2) patients who did not strictly adhere to this ratio and occasionally indulged in excess of carbohydrate often escaped acetonuria, though they developed glycosuria, (3) with a little sugar in the urine, the patient felt better, (4) with the help of Insulin, carbohydrate could be raised and fat lowered out of all relation to the formula with a great increase in both safety and well-being of the patient.

General Remarks on the Diabetic Diet

Before Insulin was discovered, several clinicians particularly Marsh, Neuburgh and Petren (Sweden) had observed that fat when given in amounts, even a little more than permitted by the ketogenic-antiketogenic ratio was able to control glycosuria, particularly when the caloric value of the diet was kept low, they formulated diets (Marsh & Neuburgh) which contained relatively large amount of fat with protein and carbohydrate greatly restricted. Diets based on the principle, high fat—low carbohydrate have nowadays been gradually replaced by diets which contain larger amounts of carbohydrate (as much as 200 gms) with proportionately less fat (upto 50 gms) as it was found (1) that with high fat diets, cases of acidosis were more frequent (2) that excess of fat strongly predisposed to arteriosclerosis, (3) that because of its low caloric value, it was difficult to maintain the weight of the patient (4) and that the patients did not adhere to such a diet for a long time because of its monotonous nature.

For reasons named above, and since its minimal physiological requirement is not precisely known, it is considered desirable that the amount of fat in the diabetic diet should not radically differ from the amount ordinarily taken in health viz 80 to 100 gms although it is possible and is at present advocated to give as small a quantity as 50 gms per day.

Before instituting dietetic treatment it is necessary to make a correct diagnosis and to ascertain the degree of severity of the disease lest the symptoms may be masked by excessive and unnecessary restrictions.

The chief aim of treatment in diabetes is to effect a balance between carbohydrate tolerance and the appropriate diet. The first factor is not known but it is possible to prescribe diet that not only has a fixed but known value. Thus the prescribing of a known diet forms the starting point of treatment and then by trial and error the exact diet which will balance carbohydrate tolerance completely, is found out. If with this diet, the weight and the normal activity of the patient are not maintained, then the aid of Insulin is to be sought for. In mild cases a simple restriction of carbohydrate in the food is all that is necessary. Such a patient should be given a list containing articles of food which he may eat, and those which he must not eat except in such measured quantities as ordered. The possibility that these cases may become more serious must be remembered and if sugar appears in the urine after an evening meal stricter methods should be adopted.

In severe and very severe cases there are two possible ways to commence the treatment, viz (1) the patient is at once put on a diet which in consideration of his height, age, built and his normal work, would meet his caloric requirements (Maintenance diet). If the urine on such a diet does not become free from sugar in a few days, Insulin has to be given. (2) The patient undergoes a brief period of undernutrition which when the urine becomes sugar free is followed by a rapid increase in diet. If diet alone fails to keep the urine sugar-free, Insulin is to be given. Treatment during the days when the increase in diet is made, becomes a problem of watching the urine and gradually building up the diet by adding small amounts of carbohydrate, then of protein and fat and increasing or decreasing the Insulin dose, depending upon whether the urine is sugar-free or not. (Note —Systems of Graham's "ladder diet" and Lawrence's "line ratio diet" are based on this principle)

In most cases, the former method is found to be comparatively quicker, more suitable and free from risk of acidosis which may likely occur in the latter starvation method. But if the patient strongly objects to the injection of Insulin or if the mild character of the disease suggests that Insulin may not be necessary, the latter method may be employed with advantage.

Planning of diet and preparation of menus form by themselves a separate subject and need not be considered here, but a few practical hints may be found useful. (1) When planning diet and preparing menus regard should be paid to food combinations and their effect on digestion. Food should not throw the least burden on the digestive organs which may otherwise cause an upset in sugar tolerance obtained after some labour.

(2) Diet must be such as would meet all the requirements of the body and supply the food constituents in such forms as would be attractive and suit the patient's constitution, tastes and habits. However the adequacy of the diet on no account should be sacrificed.

to patient's prejudices or his economic condition (3) In the case of reducing diets, strict insistence on the minimum intake of food should be maintained. A small amount of extras may mean failure to lose weight (4) In diabetics as in normal persons, there is extreme variation in the amount and type of food required and the best diet for a particular patient must ultimately be found by means of trial and error. For this reason the practice of using labour-saving standard is to be deprecated. Such fixed diets may be compared to ready-made clothes fitted to the owner. They lack variety and are inelastic and boring to the patient if continued week after week. The menus of diabetic patient should provide a sufficient variety of dishes. For this purpose, however, knowledge in practical dietetics as well as cooking is essentially necessary. Conversion of diet-prescriptions which call for gms of carbohydrate, protein and fat into the menus is not difficult, and the patient can soon learn to do it for himself. For this purpose, it is essential to have at hand "tables of food values" showing in percent the carbohydrate, protein and fat* (5) Attention must be paid to include in the diet sufficient quantity of protective foods such as milk, butter and eggs, and first class proteins together with plenty of leafy and green vegetables and fruits, so as to include enough quantities of vitamins, minerals and essential unsaturated fatty acids. If found necessary vitamin concentrates especially B in the form of marmite, bemax, or betaxin, may be given. Vitamin B₁ is nowadays believed to exercise great influence on carbohydrate metabolism, (Vorhans J A M A, 16th Nov, 1935). With high fat diet, calcium and phosphorous are likely to be inadequate and should be supplemented.

Carbohydrate should never be given in concentrated form but a large part of it should be obtained in the form 5%, 10% or 15%, vegetables and fruits. They are of distinct value in giving the necessary bulk to the food and to provide sufficient vitamins and minerals.

If the amount of carbohydrate in the diet is liberal oatmeal, potatoes, and even plantains may be given. Biscuits and whole wheat bread of known weight may be allowed in small quantities, special diabetic bread of low carbohydrate value may be ordered. Potatoes are generally to be preferred to rice or bread because (1) they have a higher satiety value (2) they are more convenient to bargain and (3) they leave an alkali residue, unlike rice. Sweets, cakes, pastries, jellies and syrups may be permitted within very narrow limits. They are more appeasing and permit the patient to feel more comfortable than a diet of starch of a similar caloric

* Tables of food values are found in the following —

- (1) F. H. Lilly's Diet Chart
- (2) The Chemistry of Flesh Food and their Losses in Cooking (Report No 187)
- (3) Nutritive Value of Fruits, Vegetables and Nuts, (Report No 213)
- (4) Health Bulletin No 23, (Govt of India Press) for Indian Foods

value Sweets and fruits should be served as desserts after a meal but never in between the meals Salted almonds or nuts may be added in small quantities to a fruit salad

Unsugared tea or coffee with a little milk, meat extracts, marmite and other clear soups may be given Unsugared lemon-water and salads without dressing would complete the diet Alcohol in any form should always be avoided

(6) It has been found that sugar tolerance is much improved when meals are frequently taken and are of low caloric value Four meals a day are therefore preferred to two If they are prepared with care and skill they will provide a menu of a large number of varied dishes that would create appetite and would prevent the patient from breaking over Diabetic diet without Insulin should be so arranged that the carbohydrate is evenly distributed between meals When Insulin is given, the larger amount of carbohydrate is given after injections

(7) Articles of food should always be simple and of known value and must be simply prepared The food should never be highly seasoned as the spices besides blunting the taste for good food, may exert an unfavourable effect on digestion and possibly on pancreas Bulky food should be given preference over concentrated as that gives more satisfaction to the patient

(8) The food making up the prescription for a diabetic may have to be considerably modified according to the condition of the patient, but in all cases before any change is made, urine examination must always be invariably made In the case of an acute illness fluid diet may be all which a patient can take at first If he is taking Insulin, it along with the usual amount of carbohydrate must not be stopped, nor its dose altered In case of indigestion the type of food used and the hours of feeds may be modified just as in the case of a normal person The bulk of the diet will have to be reduced, and instead fruits such as apples, and oranges may be given Some times when extra exercise is taken within a few hours of Insulin, extra carbohydrate such as 6 to 8 ozs of milk, 6 ozs of orange juice or 1 or 2 biscuits may be given to avoid hypoglycaemia

(9) A little appearance of sugar now and then must not be the cause of anxiety and fretting provided the patient feels fit and comfortable Extreme introspection or over anxiety is too heavy a price to be paid for a normal urine and at least in the case of certain patients, laxity would be much desirable After all, the test of a good treatment is whether the patient feels absolutely fit and is able to do his normal work and maintains a constant weight

Critical Notes and Abstracts

CARCINOMA OF STOMACH

Boyce, (Carcinoma of Stomach in a large general hospital, JAMA, 117, 1670, Nov 15, 1941), finds that of 1921 cases treated for carcinoma of the stomach from January 1922 to January 1941 at the Charity hospital of Louisiana, only 619 were explored and the non-surgical deaths in the series (366) exceed by over 50%, the surgical deaths (235). The state of affairs still remains the same in spite of the fact that as early as 1900 W J Mayo voiced the opinion that a mere suspicion of carcinoma of stomach should be an indication for surgical exploration of the abdomen.

He points out that out of every 30 patients admitted for cancer of stomach only 10 are operated upon, and of these only 2 are submitted to gastrectomy and eventually only 1 leaves the hospital alive. All through these years the mortality of gastrectomy has remained the same (56%) though figures from other private clinics are lower. He attributes the high mortality in his series to the large proportion of Negroes represented (nearly 45%)—people who are notoriously indifferent to early manifestations of disease.

The symptoms in his series were protean, representing various kinds of dyspepsia and indigestion. Pain, though regarded as unusual was present in 50% of the cases. Just over 25% of the cases presented histories suggestive of ulcer. Nearly a tenth of the cases were of a lower age group than what is usually considered as the cancer age. The majority of these in the lower age group were Negroes (25 out of 38) substantiating Gaither's statement that cancer develops at an earlier age in the negro than in the white.

Improvement in the outlook will lie in the realisation that indigestion however mild after middle age may be indicative of a serious condition like cancer. These cases would need, test meals, roentgenologic and gastroscopic examinations facilitating earlier diagnosis. Physicians who undertake the treatment of supposedly benign ulcers and functional dyspepsia should be sure of their ground. It has to be realised that in the type of cancer which masquerades as ulcer the symptoms are relieved by medical treatment and the patient is likely to slip away or lose valuable time before coming for operation. Two of the elderly patients in his series had symptoms suggestive of chronic appendicitis and had been subjected to an appendicectomy by the Macburney's method and these were later proved to be cancer stomach. Similar cases have been

reported by Ochsner and a suggestion is made for greater caution in diagnosing chronic appendicitis in the cancer age. The basic problem for improvement in the outlook will be in how soon after appearance of symptoms, the patient presents himself to the physician, and how soon afterwards the physician turns him over to the surgeon for exploration—particularly when the possibility of cancer cannot be ruled out in any other way.

Waltman Walters and his colleagues, (Malignant Lesions of the Stomach. *Ibid* 117, 1975, Nov 15, 1941), in reviewing the cases of malignant lesions of the stomach admitted to the Mayo Clinic during the years 1907 to 1938 (inclusive), found that though over half the cases presented the usual symptom complex of dyspepsia associated with various grades of decline, about a third of the cases who had resectable carcinoma had symptoms suggestive of ulcer, and in another third the ulcer syndrome appeared as the initial manifestation. About 80 per cent of the cases in which the ulcer syndrome appeared as the initial symptom had temporary effective relief from pain, etc., on a medical regime suggesting benign ulceration.

Recent advances in roentgenologic technique have led to greater precision in diagnosis. Although only in 1% of the cases of resectable lesions was there a failure to report any lesion, nearly 10% of cases with resectable cancers were reported as gastric ulcers.

Of the 11,000 patients who were diagnosed as malignant lesions only 58% were explored and in only 26% of the total the lesion was found resectable. 21.4% survived the operation and the five year survival rate was 12% of the total. The five year survival rate for the resected patients approaches that of the normal population. For patients under 40 years of age the operative mortality was very much lower than in correspondingly higher age groups, although the five year survival rate was only 25.1% contrasted with 29% for people of all ages. The lesion was found to be sarcoma in 110 or 1.7%. 68 of these were submitted to resection with a mortality rate of 13.2%. In contrast to the 6.9% of cases of carcinoma which were under forty years of age. Nearly 24.5% of cases of sarcoma were less than forty years of age.

The authors conclude that partial gastrectomy affords an excellent means of treating cancer of the stomach. The mortality of the operation considering the mortality of the disease is low. The survival rate after operation approaches that for the normal population. It is pointed out that cases with persistent dyspepsia should be submitted to roentgenologic and gastroscopic examination to exclude intragastric lesion and medical treatment of an ulcer type of dyspepsia should not be instituted before determining the exact nature and site of the lesion.

NEPHROTIC SYNDROME

It has been assumed by most physicians, that the therapeutic efficiency of acacia in nephrotic syndrome is due to increased colloid osmotic pressure of the serum produced as a result of injections of acacia. The review of the experimental work on this aspect of the problem reveals contradictory results in the hands of different observers though with regard to the concentration of serum proteins, the results are more uniform in that they show a diminution of the concentration of serum proteins after injections of acacia. The authors, (A Grondsmit, M W Binger & M H Power, *Acacia in the treatment of nephrotic syndrome—Influence of intravenously injected acacia on concentration of serum proteins and on colloid osmotic pressure of the serum*—*Arch Int Med*, 68 701, Oct 1941) of the present work studied the concentration of serum proteins and colloid osmotic pressure before and after injections of acacia.

It was found that the critical colloid osmotic pressure below which there was appearance of oedema was somewhere about 166 mms of water. In general, the colloid osmotic pressure was dependent upon the concentration of serum proteins (approximately a pressure of 60 mms of water for 1 gram per 100 ccs). After injections of acacia solution there was an apparent increase in the colloid osmotic pressure in some case, in others there was a diminution and in an intermediate group it was unchanged. There was a diminution in the concentration of serum proteins (averaging — 22 per cent in 27 cases). No correlation between the increase in the concentration of acacia and the diminution of concentration of serum proteins could be established. The concentration of serum proteins before administration did not seem to be related to the subsequent relative decrease either in the group with lowest initial colloid osmotic pressures. Increases after injection of acacia were more frequent and frank decreases were absent. In the group with high initial colloid osmotic pressure decreases outnumber the increases.

In the 28 patients studied, there was disappearance of oedema in 20. Five patients had no oedema to start with. They conclude that the colloid osmotic pressure of serum may increase, decrease or remain unchanged, and the beneficial therapeutic response did not seem to be related to the changes in colloid osmotic pressure produced after injections of acacia.

It was shown by the authors, (A Grondsmit, M W Binger, & N M Keith. *Acacia in the treatment of nephrotic syndrome with special reference to excretion of chloride and water* *Arch Int Med* 68 513, Sept 1941) elsewhere that the main defect in nephrotics relates to the inability of the patient to excrete all the sodium chloride and water ingested in 24 hours. The retention and consequent accumulation of these substances in the lymph and tissue spaces results in the appearance of the oedema. As intravenous injections of solutions of acacia have a decided beneficial effect in clearing up

the oedema, the possibility of the substance acting through increased excretion of sodium chloride and water had to be considered. Experiments on healthy dogs reported elsewhere showed that there was an increase in the excretion of sodium chloride (ranging from 4 to 352 per cent with an average of 189 per cent) after injections of acacia. In view of these results the authors studied the concentration of sodium chloride in urine and absolute quantities of sodium chloride excreted before and after injections of acacia, in 4 patients. They also studied one patient who was treated on potassium nitrate alone without injections of acacia. It was found that following injections of solutions of acacia in some, there was an increase in the concentration of sodium chloride in the urine, and there was an increase in the absolute quantities of sodium chloride and water excreted in 24 hours. The administration of potassium chloride after injections of acacia did not seem to alter the amount of sodium chloride excreted. In one patient the amount of sodium chloride excreted was definitely lower after an injection of mercurial compound (Esidrone) than after injections of acacia. In some cases the concentration of sodium chloride in the urine was unaltered after the injections, though the absolute quantity of sodium chloride lost in 24 hours was definitely increased.

The mechanism of action of acacia resulting in increased excretion of sodium chloride and water as unexplained at present. The increase in the volume of circulating blood produced after injection of acacia does not seem to be responsible as there are conditions like congestive cardiac failure where plethora is associated with oedema. If one takes into account the current concept of renal excretion as one of glomerular filtration followed by tubular reabsorption, the defect in nephrotic syndrome would be related to some defect, (increase) in reabsorption of water and sodium chloride by the tubules, as there are no disturbances in glomerular function in these cases. How the diminished colloid osmotic pressure is related to the disturbed tubular function is difficult to explain. It seems probable according to the authors that acacia acts by re-establishing normal rate of tubular reabsorption of sodium chloride and water.

P R

PROTHROMBIN DEFICIENCY IN PULMONARY TUBERCULOSIS

Among 106 cases of active and chronic Pulmonary Tuberculosis studied by Sheely (J Amer Med Assn (1941) 117 1603) in regard to the concentration of prothrombin in the blood a significant deficiency of prothrombin was found in 51. Among the patients 73% with minimal, 60% with moderately advanced and 9.6% with far advanced tuberculosis had a prothrombin concentration within the normal range. 68.5% of those with far advanced tuberculosis had a prothrombin concentration below 59% of normal. There was no constant relation between the prothrombin concentration and the sedimentation rate. The status as to prothrombin level appeared to con-

cide with the clinical and Roentgenologic status of the majority of the patients. There appeared to be a relation between the prothrombin concentration in the blood and the degree of toxæmia as measured by clinical standards in Pulmonary Tuberculosis. There seems to be a less certain relation between the prothrombin level and the extent of the active tuberculous involvement. In chronic inactive tuberculosis, regardless of the original extent, the prothrombin concentration is usually within the normal range.

It is suggested that the prothrombin concentration should be determined in every case of Haemoptysis in Pulmonary Tuberculosis. In 4 cases of frank haemoptysis with associated prothrombin deficiency, the elevation of blood prothrombin level on administration of vitamin K orally or parenterally was a likely factor in the control of the Haemoptysis.

J C P

A STUDY OF THE NORMAL BLOOD PRESSURE IN INDIANS

So far we know the standards of blood pressure for normal individual in this country have not been worked out. This study was carried out on 10,000 persons from different parts of India (Sir R. N. Chopra et al. *Ind. Med. Gaz.*, 1942 (Jan.) 21,) on normal individuals between ages of 15 and 30 years, from both rural and the urban populations. The blood pressure was taken by means of mercury baumanometer, auscultatory method being employed to the readings. These were 8,105 males and 1,895 females from all communities from North and South coast of India. Figures obtained are compared with those obtained in Europeans.

The average Systolic pressure in Indians is lower than that in Europeans. For any age range this difference varies from 5 to 14 mm Hg. About 53.7 per cent of Indians have their Systolic pressure between 100 and 119 mm Hg against 20.5 per cent Europeans for the same range. For higher ranges e.g., 120 to 139 mm Hg the percentage of Europeans increases up to 54.6 against 32.9 only for Indians.

The average Diastolic pressure of Indians is also lower than that of Europeans. This is approximately 8 to 9 mm of Hg less. The pulse pressure naturally is also proportionately low but between the ages of 35 to 60 years it attains almost the same height as in Europeans.

Amongst the various Communities in India, it has been found that the people of the north (Punjab, U.P., and Delhi) have higher Systolic and Diastolic pressures than the people of the east (Bengal, Bihar and Orissa) and south (Madras). The bracing climate of the north, better diet and higher standard of living would possibly account for this difference.

People on mixed diet have slightly higher blood pressure than those on a purely vegetarian dietary.

J C P.

A Short Review OF THE FOURTH ADDENDUM (Oct 1941) TO THE B. P. 1932

By

C C MERCHANT

M B B S

(From The Pharmacological Dept, Seth G S Med College, Bombay)

The first, second and third Addenda to the British Pharmacopoeia 1932 were published in 1932, June 1940 and January 1941 respectively. The fourth Addendum was published on 1st October 1941 and became official from the same date.

The fourth Addendum, like the second and third Addenda, is obviously an effort to deal with conditions arising from scarcity of dry supplies as a result of war, and in particular to effect economies in the use of materials like glycerine, sugar, alcohol, potash salts etc, which are in short supply or those which are too costly to prescribe. In this addendum are included a number of preparations which in pre-war days were obtainable only from Germany. Till the publication of the B.P. 1932, very little consideration was given to include in the pharmacopoeia and to officially recognize certain foreign preparations which were freely available and widely used in therapeutics under proprietary trade names. In the newer Addendum, evidently an attempt is being made to get rid of the strong foothold which German chemical manufacturers had secured in the drug market not only in England but all over the world.

Another noticeable feature is the inclusion in the Addendum of a certain number of compounds, the manufacture of which either was hitherto restricted by patent rights or is still covered by patents.

In the fourth Addendum, a number of new monographs have been added whilst, in a number of cases, alterations, additions or omissions have been made in the existing monographs, i.e., those contained in B.P. 1932 and the subsequent three Addenda.

Below are given in brief, details of the monographs pertaining to newer drugs, officially recognized in the fourth Addendum —

1 *Acidum Mandelicum* — White crystals, soluble in about 7 parts of water. Dose 30-60 grains. This drug was introduced as an urinary antiseptic in 1935, is not employed as such, as it is irritating to the stomach. It is usually prescribed mixed with sodium bicarbonate or in the form of its ammonium or calcium salt.

2 *Acidum Nicotinicum* — Chemically identical with the factor in Vitamin B₂ which prevents human pellagra (P.P. Factor), Soluble in water. Dose $\frac{3}{4}$ —1½ grains (50—100 mgm.)

3 *Benzylis Benzoas*—Introduced for its curative action in Scabies Insoluble in water, but soluble in 90% alcohol and is insoluble in glycerine In doses of 5-8 minims, the drug may be used as an anti-spasmodic, for instance, in the treatment of asthma It was introduced in therapeutics as the proprietary preparation "Spasmodin"

4 *Bismuthi Subgallas*—It is not a new preparation, was introduced into medicine as the proprietary "Dermatol" It is used externally as an antiseptic dusting powder f i in piles, and internally in doses of 10-30 grains as an astringent in the treatment of enteritis

5 *Digoxinum*—A crystalline glucoside obtained from the leaves of *Digitalis Lanata* It was introduced as the proprietary "Digoxin" and its manufacture is still controlled by patent rights Digoxin is almost insoluble in water, but soluble in 70% alcohol

Dose recommended is 1/120 to 1/60 grain by intravenous injection By oral administration, the initial dose given in order to obtain the characteristic Digitalis effect is 1/60 to 1/40 grain, and the effect is maintained by giving 1/240 grain twice daily

6 *Ephedrina*—This alkaloid (base) is introduced on account of the wide use of its oily solutions f i as nebuloe Ephedrine (base) is soluble in about 20 parts of glycerine, in about 25 parts of olive oil and in about 100 parts of liquid paraffin It is readily soluble in 95% of alcohol The B P dose is ¼—1½ grain

7 *Injectio Calci Gluconatis*—This is an approximately 10% solution of calcium gluconate in freshly prepared distilled water making a super saturated solution Dose—150 to 300 minims Calcium gluconate was included in the First Addendum (1936) to the B P 1932

8 *Injectio Nikethamidi*—This preparation is still popularly known under the proprietary term "Coramine" It contains 25% of Nikethamide Dose—30 to 60 minims by subcutaneous or intramuscular injection (as a medullary stimulant), and 75 to 240 minims administered intravenously as a convulsant

9 *Injectio Procaine et Adrenaline*—It contains

Procaine Hydrochloride	2 0 gms
Sodium Chloride	0 5 gm
Chlorocresol	0 1 gm
Solution of Adrenaline Hydrochloride	2 0 mls
Sodium Metabisulphite	0 1 gm
Distilled water, freshly prepared to make	100 0 mls

It may be noted that chlorocresol and Sodium metabisulphite are added as the preservative and anti-oxidant respectively

10 *Injectio Quininae et Urethani*—This solution contains in 100 mls, 12 5 gms of Quinine Hydrochloride and 6 25 gms of urethane with 0 1 gm of chlorocresol as the preservative The dose by intravenous injection, as a sclerosing agent is 8 to 75 minims Solid

matter is likely to separate on long standing but it will redissolve by warming. The syringe used for injecting the solution should preferably be warmed previously.

11 *Injectio Sodii Morrhualis*—It is a 3% solution of Sodium Morrhuate with the addition of 0.1% of chlorocresol. Dose—8 to 75 minims administered intravenously as a sclerosing agent in the treatment of varicose veins.

12 *Liquor Sodii Hydroxidi*—It is intended to replace solution of Potassium Hydroxide of the B.P. It contains 3.56 per cent w/v of NaOH.

13 *Magnesi Trisilicas*—The dose is 5 to 30 grains. Its use is well known in the treatment of hyperacidity of the stomach.

14 *Morphinae Sulphas*—This salt of morphine was official in the B.P. 1898, but was omitted from all subsequent editions of the B.P. It is now once again recognized officially probably because of its suitability for the preparation of injections. It is more soluble than the hydrochloride and more stable than the tartrate. Dose 1/8 to 1/3 grain.

15 *Pamaquinum*—This compound is said to be identical with the well known German proprietary preparation "Plasmoquin." The dose is 1/3 to 3/5 grain. The method of manufacture is protected by patents. Solely used in the treatment of malaria.

16 *Paraffinum Liquidum Leve*—Light variety of liquid Paraffin is useful in the preparation of oily spray solutions. Its Kinematic viscosity is now given as not greater than 33.0 centistokes at 37.8 C.

17 *Phenylhydrargyri Nitras*—Prepared by Otto in 1870, may be used as a skin disinfectant. It is very slightly soluble in water, but dissolves in about 160 parts of boiling water and is soluble in glycerine and fixed vegetable oils. It is introduced in the addendum as a bactericide to be used in one of the special processes employed in making parenteral injections.

18 *Proflavinæ Sulphas*—At present, proflavine is preferred to Acriflavine as an antiseptic, as the former is compatible with physiological solution of Sodium Chloride and is believed to be a slightly more active bactericide, less toxic, and possibly to possess homeostatic properties. Hence it is included in the Addendum. Proflavine is soluble in about 300 parts of water or in 10 parts of glycerine.

19 *Sodii Metabisulphis*—The chief use of this compound is as an anti-oxidant in the preparation of solutions containing such substances as adrenaline. It dissolves in about 2 parts of water and must be stored in well-closed containers.

20 *Sodii Morrhuas*—Originally used in the treatment of leprosy and tubercle, Sodium Morrhuate is now employed entirely as a sclerosing agent in the treatment of varicose veins. It occurs as light brown granules or powder having a slightly fishy odour and a

slightly acrid taste It must be kept in well-closed containers, protected from light and stored in a cool place

21 *Sodii Sulphas Exsiccatus*—Although dried sodium sulphate is in common use as an ingredient of effervescing aperients, its introduction in the Addendum seems to be meant as a substitute for dried magnesium sulphate Does 15-120 grains

22 *Sulphanilamidum*—This is the first and only preparation representing the Sulphonamide group of drugs so commonly used in recent years It occurs as colourless crystals or as a white crystalline powder, having a taste which is at first slightly bitter and afterwards sweet It is soluble in water 1 in 250 Dose is stated to be 8-15 grains, though this drug is given in widely varying dosage to treat various conditions

23 *Suranum*—This compound originally introduced under the proprietary name Bayer 205 or Germanin (1920) and known in France as Fourneau 309 and in Great Britain as antrypol—is used in the treatment of trypanosomiasis Two biological tests have been described, one for the absence of undue toxicity and the other for therapeutic potency The dose is given as 15-45 grains by intravenous injection, the drug being dissolved in the requisite amount (10 cc for every 15 grains) of physiological solution of sodium chloride immediately before use

24 *Unguentum Hamamelidis*—Has been added to the list of official ointments and contains 1 part of the liquid extract, 6 parts wool fat and soft paraffin 3 parts

25 *Unguentum Hydrargyri Dilutum*—This ointment contains 10% of mercury and is prepared by mixing 1 part of ointment of mercury with 2 parts of simple ointment There is a foot note to the monograph that when mercury ointment, mercurial ointment or blue ointment is prescribed or demanded, dilute ointment of mercury shall be dispensed or supplied, unless on enquiry, it is ascertained that ointment of mercury is required

On the other hand, the synonym "mercury ointment" for *Unguentum Hydrargyri* has been deleted

Besides, in this addendum, amendments have been made to several existing monographs, and also a number of changes in the Appendices of the Pharmacopoeia have been included, the most important being in connection with Appendix XVI—pertaining to methods of sterilization which have been revised in the light of more recently obtained information The process of tyndalization—i.e., sterilization by discontinuous heating as laid down in the B.P 1932 being found unsatisfactory—has been omitted and has been substituted by sterilization by heating with a bactericide like chlorocresol (0.2%)

Book Reviews & Notices

THE ART OF LOVE AND SANE SEX LIVING (Based on Ancient Precepts and Modern Teachings) By A P Pillay, O.B.E., M.B.-BS Published by D B Taraporevala Sons & Co, Bombay, 1942 Pages 530, with 80 illustrations and 92 photographs specially taken for the book by Dr S H Marathe, M.B.B.S Price Rs 10/-

In India there is as much ignorance about sex matters as anywhere else in the world. The belief of some Western writers that the people of the orient were or are superior to the occidental races in the knowledge of sex or in sexual prowess does not appear to be based on any observational facts. Social workers and practising physicians in India are only too familiar with the havoc wrought by the abysmal ignorance of parents, teachers, priests, and newly married or old married couples in matters of sex. Even the medical men are no better than most lay persons in this matter, as there is no place for instruction in sex matters in the orthodox medical training. All these need to be instructed in sexual functions and hygiene, fertility and contraception, sex abnormalities and diseases. In the West the subject has been extensively studied during the last fifty years. The studies of Ellis, Freud, Stekel, Ferenzi, Adler, Pouillet, Van de Velde, Robinson and others have produced a mass of knowledge which it is necessary to impart to the man in the street in a simple straightforward language.

Dr Pillay's manual written in a simple language, outlining the modern conceptions of sex life, is an attempt to supply this need. As the author says in his preface, the book is meant "to instruct and not to amuse" (We would have liked less of the quotations from the ancient literature which only serve to amuse rather than instruct, and more emphasis on the modern scientific facts. However, we cannot complain about it as the author has fortified himself by his subtitle that the book is "based on ancient precepts and modern teaching") "The more I come into clinical contact with sex disorders and marital maladjustments, the more I am convinced that it is not treatment that these patients need but the right kind of instruction in biological facts, and this is what I have attempted to impart in this book. It should, therefore, prove helpful to the old and the young. To the old it will help to make practical adjustments as regards their sex lives and problems. To the young it will save a lot of misery if they begin life knowing scientific facts on sex life and sex behaviour. They can then sail clear of emotional tempests and rocks on which many young lives are now often wrecked."

In this aim the author has fully succeeded. The book contains much valuable practical advice, based on the author's extensive clinical experience. It also contains a long chapter on Exercises to acquire sex efficiency and to cure sex deficiency, which is well illustrated by photographs taken by Dr S H Marathe. The chapter on Control of Conception is well written, different contraceptive methods are compared and evaluated. The author has described the Vitamin C Test for ovulation which appears promising and should engage the attention of the Gynaecologists. With the assistance of Mr M J Sethna, Bar-at-Law, the author has written a chapter on Legal aspects of Marriage and Sex, which gives much useful information regarding the marriage Law and Custom among the Hindus, the Mohammedans, the Parsis and the Christians, much of which will be 'news' to many medical readers.

There is a complete glossary of difficult and technical words, a short bibliography and a subject index at the end. The book is well printed and produced. Medical practitioners can recommend this book to their patients who are worried by sex problems and who need a presentation of the modern views on these matters in a simple and helpful way.

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LIVERGEN

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 Pichotia seed, Licuagreek,
 Hygrophila Spinosa
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Let us remember

JEAN NICOLAS CORVISART

1755-1821

A Creative Genius of Practical Bed-side Teaching

The eighteenth century was the age of the French renaissance. The writings of the Encyclopaedists, Descartes, Rousseau, Voltaire and others had stirred the French people as never before. The new ideas in literature and science had produced a new generation of sceptics who will have nothing to do with the old tradition, and who brought about a revolution not only of government, but of ideas, which altered the future not only of France but of the whole mankind. In this age of enlightenment and turbulence, Corvisart was born in a small French village of Dricourt on February 15, 1755. His father was a solicitor to the crown and he was originally destined for the legal profession. He spent his student days with his pastor uncle at Vimille. At the age of thirteen he matriculated at the College of Saint Barbe. In the school he showed no evidence of intellectual superiority. Described as a "lazy, mischievous, and quarrelsome" student, he only distinguished himself by vigorous feats of body. His father took him in his office to study law. Corvisart did not like law-studies, found the task of copying legal documents irksome, and spent most of his time in the Latin Quarter, listening to one lecturer or another. There the lectures of Desault, at the Hotel-Dieu, the largest hospital in Paris, fascinated him and he forsook law and became a medical student under Desault. This angered his father and he was expelled from the paternal home. He applied for a residential

position at the Hotel-Dieu to insure board and lodging, secured it and settled down to study medicine

In 1782 he qualified as a doctor and was appointed parish physician at a minimal salary. Before long there was a vacancy at the Hospital Necker and he applied for it. He presented himself before the governing body without wearing a wig. His qualifications and recommendations were satisfactory but they would not appoint him unless he wore a wig. Corvisart refused to give way on this point, and in a letter declining the post wrote "Respect for outward signs must not degenerate into superstition."

In 1785, he became Doctor—regent of the Paris Faculty of Medicine and associated himself with the chair of anatomy at the Hotel-Dieu. In 1788, he succeeded Rochefort as a physician to the Charite Hospital. At this time the Viennese school of medicine was at its height and Corvisart decided to go to Vienna to obtain first hand knowledge at the hands of the Viennese masters. In Vienna he studied the new method of percussion which was introduced by Auenbrugger, and which was not heard of in Paris at that time. He writes

"Percussion made a strong impression upon me, and I think that since then I have practised it unceasingly, whether in obscure diseases of the chest or in those that were simple and easily understood. It never led me astray if the condition of the patient was such as to allow me to make full use of it. On the other hand, I must frankly admit that I have known of many grave errors in diagnosis on the part of those who knew nothing of percussion or neglected it." He studied and wrote of other Viennese writers and in 1797 translated the Aphorisms of Max Stoll in French, called "Aphorisms on the Knowledge and Cure of the Fevers." In 1802 he translated the Aphorisms of Boerhaave. In turn his favourite pupil, Laennec, published Corvisart's aphorisms. One of his pupils, F. V. Merat had taken down detailed notes of Corvisart's lectures and sayings in the wards and collected them in a manuscript "A Course of Clinical Medicine by Baron Corvisart with Aphorisms Concerning Certain Diseases, collected from the lec-

tures of this Professor" This manuscript was recently found in the library of the Académie de Médecine of Paris and the third section in it which contains the aphorisms was published by Paul Busquet, the librarian, in 1929

Corvisart practised percussion diligently and developed its use In 1808, he translated Auenbrugger's treatise, *Inventum novum*, adding his own comments and observations, and it is this translation which brought the method of percussion before the medical profession and which has since then become the inseparable part in every clinical examination

In 1797, Corvisart became Professor of practical medicine in the Collège de France Here, he developed the art of clinical teaching For twenty years he taught clinical medicine and trained a number of young physicians. His methods were so novel that a large number of students were attracted to his demonstrations and his fame spread all over Europe He disliked formal lectures and preferred informal oral teaching at the bedside In the preface of his translation of Stoll's aphorisms he states

"The preparation and dictation of formal lectures is an art of the middle ages which involved great expenditure of time, often concealing the real meaning, and giving but little instruction An informal oral presentation or conference is more rapid, more alive, makes a more lasting impression, and allows the consideration of many more subjects in a given time"

Sigerist describes his method of clinical teaching as follows "In the morning he went his round at the Charité, accompanied by a train of students as he moved from bed to bed, examining each patient with the utmost care "The medical training of the senses" was his watchword and his programme Students must learn to use their sense-organs. Everything depended upon accurate observation By the bedside of the sick theory was silent, for the only thing that mattered was to see and to hear Corvisart himself was a marvellously keen observer We are told that one day looking at a portrait, he said "If this picture is a faithful one, I cannot doubt that the original must have died of heart disease" Enquiry showed

that such had been the case. When a patient died in the clinic, a careful examination of the intact body was first made. Then came the autopsy, and immense was the delight of the doctor and his pupils if this confirmed the diagnosis. Still more instructive, however, were instances in which discrepancies arose. They gave Corvisart an opportunity of showing in masterly fashion how and why he had erred, and of explaining what was to be learned from these new observations. In the evenings he delivered theoretical addresses at the College de France, speaking extempore as a rule, and discussing cases which had been treated in the morning."

These informal lectures became immensely popular because they were based on personal experience of the speaker and free from the dead weight of theories of the middle ages. His pupils or assistants became the leading physicians in Paris hospitals. His pupil Laennec, adorned the Necker hospital where he developed that technique of auscultation and perfected his master's method of clinical observation and post-mortem study. Bayle, Cuvier, and Dupuytren were all inspired and patronized by him. Paris became the Mecca of clinical teaching, and attracted brilliant pupils from the Continent, the British Isles and the United States of America.

Apart from the translations mentioned above, Corvisart wrote, "The Diseases of the Heart and Great Vessels," published in 1806. Applying his method of study to the cardiovascular system, Corvisart achieved wonderful results. He insisted on the frequency of organic heart diseases and differentiated them from the functional heart diseases. He studied the size of the heart by the new method of percussion and made a thorough study of cardiac insufficiency. This work became very popular, went through many editions and was translated into English and became a standard text book in England and America for many years.

In 1807, Corvisart became physician to Napoleon I. It is said that at the Siege of Toulon, Napoleon, then a young artillery officer, had taken the place of a slain gunner and acquired a dermatitis. Corvisart was able to cure this. Corvisart's method of asking search-

ing questions and making a thorough physical examination, appealed to Napoleon. Corvisart was always at the imperious call, and his patient was most difficult and exacting. Nevertheless, he got on well with him and became very friendly. It is said that Napoleon once said he had no faith in medicine but he had faith in Corvisart. Napoleon and Corvisart greatly enjoyed each other's company and many interesting anecdotes are told of their conversations. In one of these, it is said that the Emperor, who was in constant fear of being poisoned, literally rolled on the floor because of a slight attack of indigestion. Corvisart is supposed to have reproved him, saying, "Get up! What would be said if the master of the world were seen thus crushed by fear?" Perhaps the most famous story is the reported conversation related by Beeson, between Corvisart and the Emperor, following the birth of Napoleon's son, the King of Rome, in 1811.

"Sire," said the physician, "this child should fulfill your last wish. Consider from what a position you have arisen in less than ten years: lieutenant, captain, brigadier-general, general-in-chief, First Consul, Emperor, spouse of an Austrian Archduchess, and the father of a male child. You have reached the summit of the Wheel of Fortune and of great renown. Stop! Sire, or Destiny may desert you and then nothing remains but downfall and disaster." "Well," said the Emperor, "that was such a speech as one would expect from a native of the Champagne."

Corvisart remained loyal to Napoleon all his life. After the final defeat and exile of the Emperor, Corvisart broke down and retired within himself. He refused all offers of the new government. He suffered great financial reverses and was constantly troubled. He wrote feelingly

"I was more happy when I had only two sous a week for my simple pleasures. It will be necessary sooner or later to sell my home. I shall lose more and, in order to pay the price, there will still be some chicanery, so that I shall end my life in the midst of these petty little law-suits which, as you know, I love so well."

Corvisart seems to have always been in financial troubles. His family appears to be a liability. He paid the debts contracted by his father. He had to borrow money for his licence. He had to pay the debt of a brother and is said to have sold his silver plate to satisfy the creditors. Once he had to call the help of a friend to relieve him of an aunt, who together with her daughter and granddaughter had taken possession of his quarters in the rue St. Dominique. He wrote "Come quickly to my assistance. I do not wish to see them. I am inclined to force my tender relatives to return to Chateau Porcier or to the devil." Corvisart was married in 1793. It was not a fortunate or happy experience, and a separation was granted in 1797. His only son lived less than one year. Soon after Napoleon's exile in 1815, Corvisart had his first apoplectic stroke. He had a more severe one in 1816 which left him partially paralyzed. He retired from practice and spent his days with his friends, and in reading and in writing his memories. In 1821 a third fatal stroke occurred.

Apart from his associations with Napoleon, Corvisart will always be remembered by physicians, because of his rediscovery and popularization of Auenbrugger's method of percussion which had not attracted the attention of physicians before his time. He will still be remembered and followed as an ideal clinical teacher, who started the new school of practical bedside teaching and pathological studies, which was perfected by his brilliant pupils, like Laennec, and which has become the standard method of clinical teaching all over the world since his time.

Original Contributions

NON-SPECIFIC PROTEIN THERAPY

By

J C PATEL,

M D (BOM), F H D, M R C P, (LOND)

It is over 30 years since non-specific protein therapy was introduced, and like many other new forms of medical treatment, it has had its ups and downs. It has lost some of its former popularity, but it has gained in prestige by reason of a better understanding of the fundamental nature of the reaction which follows its use

Historical

Fernando Torres (1913), a South American, reported successful results in the treatment of typhoid fever by giving typhoid vaccine intravenously, and described the sharp reactions that followed its injection. In 1914 Dessy, Grapiolo and Fossati, Kraus and Mazza, and Ichikawa reported results of treatment of typhoid fever with typhoid vaccine both by the intravenous and subcutaneous method. They found the intravenous method gave much quicker results and noted that many cases so treated terminated abruptly by crisis or rapid lysis, and that mortality was definitely reduced. No doubt this method of vaccine treatment was originally intended as a form of specific therapy, but when Kraus and co-workers (1917) obtained similar results with colon bacillus, they opened the door to non-specific therapy in all its various forms and modifications. Ludke (1915) showed that excellent results could be obtained in typhoid with intravenous injection of albumoses. Schmidt (1916) found that intramuscular injections of boiled milk would produce febrile reactions. Since then a large number of different agents, many of them proprietary, have been advocated, some for intravenous and others for intramuscular use.

Many forms of protein and protein derivatives have been tried therapeutically. Among the more important are —

- 1 Non-poisonous proteins of animal or vegetable origin, i.e., albumin, edestin, milk and casein, serum pro-

teins either human or animal, normal serum, immune serum especially diphtheria antitoxin

- 2 Protein split products including peptone, proteose, albuminoses and histamine
- 3 Bacterial proteins and toxins, and extracts (tuberculin, Coley's fluid, etc.).
- 4 Enzymes and tissue extracts
- 5 Toxic vegetable proteins, e g ricin, abrin
- 6 Animal venoms, e g snake and bee venom
- 7 Animal—vegetable cells, bacteria (vaccines), red blood corpuscles
- 8 Malaria therapy is a form of foreign protein treatment. The protein is set free in the blood of the patient when segmentation of the malarial parasite occurs.

A great many commercial protein products have been put on the market. Three which are frequently used are —

- (1) Typhoid vaccine
- (2) Boiled milk
- (3) Diphtheria antitoxin

Methods of Administration

- 1 *Milk* Ordinary skimmed milk, either fresh or pasteurised, is boiled for 5 to 10 minutes and then cooled to body temperature. The first dose for adults is 5 cc injection intramuscularly, usually into the gluteal muscles. The dose is increased 2 or 3 cc with each injection, until a maximum of from 10 to 15 cc is reached.
- 2 *Diphtheria Antitoxin* is not given for its antitoxic property but it is an easily available form of horse serum. When used as non-specific protein, the dose is usually from 2 to 4 cc given intramuscularly.
- 3 *Vaccines and other bacterial Proteins* Ordinary stock and autogenous vaccines are given intramuscularly, and when sharp thermal reactions are desired, intravenously. Typhoid vaccine is most popular in small doses of 10 to 25 million organisms. Gonococcal vaccine for gonorrheal arthritis and streptococcus vaccines for infectious arthritis are also used intravenously.

Non-Specific Reaction

The reaction to foreign protein injections varies from an almost imperceptible one to extreme shock associated with high fever, profound vasomotor disturbance and other constitutional phenomena. The reaction depends on (1) the substances injected, (2) the dose employed, (3) the method of administration, (4) physical condition of the patient, and (5) the number of previous injections.

Intramuscular injections of protein usually excite comparatively mild reactions. There may be only some local reaction at the site of injection and constitutional reaction may be absent. Sometimes a focal reaction occurs. When milk or other protein is given in large amounts, there may be mild chill and a rise of temperature of one or two degrees, with increase in leucocytosis.

Intravenous injections of foreign proteins produce sharp and prompt reactions. They come within half an hour to one hour after injection, and with chill or an actual rigor with general ache. As the chill subsides, the temperature of the patient begins to rise. Maximum temperature of 103° — 105° F is reached usually within two to four hours after the injections, with proportionate increase in pulse rate. It is usually followed by rapid defervescence.

In acute infections such as typhoid or pneumonia, in which a temperature of 102° to 104° F already exists, the temperature during a protein reaction following an intravenous injection may sometimes go to 106° to 107° F. So the intravenous dosage for febrile patients should be about half that for afebrile individuals.

Following the injection of foreign protein there is leucopenia, but with the onset of the chill, a gradually increasing leucocytosis takes place which reaches its maximum about six hours and then gradually returns to previous levels. The increase is of polymorphonuclear type. In afebrile patients the leucocytosis varies from 12,000 to 15,000 per cmm. Blood-pressure shows a gradual rise during the chill and returns to normal during the period of perspiration.

Mechanism of the Reaction

The typical thermal reaction of protein fever can be divided roughly into three phases. Immediately after intravenous injection there is a latent stage with no symptoms, and later a stage of chill. The period from the onset of fever to the point of maximum temperature is referred to as the first or negative phase, the second or positive phase extends from the height of the fever to the return of normal temperature.

Some of the many physiological changes (Hench, 1932) that take place in the body during the protein reaction are as follows —

- 1 Alteration in basal metabolism
- 2 Peripheral and splanchnic vasomotor changes, including alterations in blood-pressure and in the calibre and permeability of arterioles and capillaries
- 3 Alteration in serum ferments, anti-ferments, antibodies and Wassermann reaction
- 4 Alterations in organic activity demonstrated by increased secretion of lymph, bile, saliva, breast milk, and menstrual flow, and by changes in the activity of the liver, gastro-intestinal tract and spleen
- 5 Alteration in the volume, specific gravity, freezing point and viscosity of the blood
- 6 Alterations in cellular elements of the blood, e.g., leucocytosis
- 7 Alterations in fragility of the blood platelets and in fibrinogen, thrombokinase, coagulation time and sedimentation rate
- 8 Alterations in the chemical constituents of the blood demonstrated by changes in the CO₂ tension of the plasma, carbon dioxide combining power, total non-protein nitrogen of the whole blood and of the serum, sugar tolerance, albumen globulin ratio, concentration of urea, uric acid, sugar fat, total serum-protein and chlorides

Which one or combination of these physiological changes is responsible for the beneficial effects that often follow protein injections, is unknown. Jobling and Paterson (1916)

thought that beneficial effects were due to the mobilization of enzymes, particularly proteases and lipases. According to Mueller (1927) the protein reaction involves a reaction of the entire vegetative nervous system which manifests itself in certain functional changes or organic activities.

While most writers stress the importance of fever in the protein reaction, Zimmer and Buschmann (1925) hold that acute conditions frequently require a fever reaction, while chronic conditions will often be best affected without any fever reactions.

Perhaps the most important function of the foreign-protein reaction is the mobilization of immune bodies in the circulating blood. Whether this is due to increased formation or to increased mobilization of antibodies it is difficult to say. It has been generally assumed that the beneficial effect of the foreign protein reaction is referable to the fever, and that up to a certain point the higher the fever the better the results obtained. There are some, however, who believe that leukocytosis that accompanies the reaction has important therapeutic value.

Untoward Reaction

Several and even fatal reactions sometimes follow the intravenous injections of foreign protein. Such occurrences, however, usually take place in patients who are already seriously ill, or who have been greatly overdosed with protein. Hench (1932) has analysed the reaction of typhoid vaccine, in most cases given intravenously, of 2,500 patients at Mayo clinic. Unusual reactions were noted in 14 cases. These were acute and subacute appendicitis, cholecystitis, enteritis, pleurisy, pericarditis, iritis, glaucoma, adenitis, vascular thrombosis and renal insufficiency. In this large series, death occurred in only three cases, a mortality rate of 0.12 per cent.

Clinical Application of Protein Therapy

The literature on the clinical application of foreign protein therapy in various diseases is so enormous that in a short review of this kind reference can be made to only a limited number of them.

Typhoid was the first infectious disease to be treated by foreign protein therapy. Millar (1927) observed that the course

of disease is favourably influenced in 60 per cent of the cases. He adds, however, that intramuscular injections are safer than intravenous injections in this disease. Holler (1917) used small doses of a 10 per cent solution of deutero-albumose, beginning with two treatments a day and later giving one treatment daily, continuing the injections until the fever was broken. In 1917 he reported 350 cases treated by this method with a death rate of only 0.5 per cent, and an average duration of the disease of only 10 days. These are the most impressive figures reported in the literature.

Pneumonia Before the advent of efficacious serum and sulphapyridine therapy, non-specific protein therapy has been tried with some success in cases of pneumonia.

Sepsis The chills and temperature reactions of a patient with sepsis bear a strong resemblance to those which follow intravenous injections of foreign protein. A number of writers have reported favourable results from this method of treatment.

Syphilis In the earlier days of protein therapy a number of investigators found it quite valuable in the treatment of the cutaneous manifestations of syphilis. With development of arsphenamine as a specific therapy it was no longer needed, but it is still used in the treatment of Dementia Paralytica and to a less extent in tabes dorsalis. It was advocated first by Wagner-Jauregg in 1917. The brilliant results obtained in this disease with typhoid vaccine and malarial therapy is indeed amazing when one considers how comparatively little benefit was gained from ordinary treatment of this condition with mercury, arsenic and the iodides.

In 1931 Wagner-Jauregg reported results in 3,000 cases of dementia paralytica treated in Vienna with malaria therapy. The results have been most impressive and have been widely corroborated by other investigators in Germany, Great Britain and America. Wagner-Jauregg was convinced that malaria therapy was much superior to other agents for production of thermal reactions and this view is now quite widely held by neurologists. There are some, however, who believe that frequent injections of typhoid vaccines are just as efficacious and certainly typhoid vaccine has practical advantages over malaria, that it does not produce anorexia and anaemia. Both relapsing

fever and rat bite fever have been used therapeutically in *dementia paralytica*. The results seem to be about as good as those obtained by others with malaria. This still further evidence that it is the febrile reaction and not the agent which produced the fever which is the essential part of the treatment.

The results of foreign protein therapy in *tabes* have not been so brilliant as those obtained in *dementia paralytica* though Wagner-Jauregg reports that the lightning pains and gastric crises are often relieved by this treatment.

Other nervous diseases It has been tried favourably in the treatment of disseminated sclerosis, in encephalitis and post-encephalitis syndromes, in *dementia praecox*, and in chorea. However, one should bear in mind that some of the nervous diseases mentioned above are characterised by alternating periods of improvement and relapse, as the improvement which may follow fever therapy may be temporary.

Acute and chronic arthritis In the field of arthritis, foreign protein therapy has achieved considerable success, and probably more articles have been written on the use of protein therapy in the treatment of various rheumatic conditions than any other subject. Miller (1930) observed that 50 per cent of the patients with acute arthritis are free from discomfort after 2 or 3 intravenous injections of typhoid vaccine and in about 25 per cent of these the relief is permanent. Cecil (1934) is of the opinion that foreign protein therapy should always be considered in the treatment of acute arthritis, especially for those cases in which salicylates have failed to give good results.

In chronic arthritis of the rheumatoid type, foreign protein therapy has not proved so satisfactory as in the acute form, though the immediate effects are sometimes quite striking. The swelling of the joints is diminished and the pain is decreased. In the majority of cases the relapse occurs sometimes in a few days sometimes after several weeks or months of comparative freedom from pain. Miller (1930) after a wide experience with typhoid vaccine in the treatment of chronic arthritis states that in the early stages of rheumatoid arthritis in which there is evidence of marked inflammation, fever therapy will occasionally give gratifying results, terminating the disease, sometimes permanently, more frequently for a few months after which

it again becomes active but often yields to a second course of treatment Campbell (1925) treated 70 cases with typhoid vaccine and noted improvement in 58, though 16 of these relapsed On summing up the remarks "Protein shock is not and cannot be regarded as an ideal method of treatment yet I am of the view that in the present state of our knowledge of rheumatoid arthritis, it offers greater possibility of success than any other treatment" This is true even today

Diseases of skin In dermatology, foreign protein therapy has been widely used and with considerable success in certain inflammatory conditions, such as furunculosis, carbuncle, and other staphylococcal infections of the skin, and to a less extent in ringworm, lupus, pruritis and the like Sometimes a persistent form of urticaria will yield promptly to boiled milk or to some form of bacterial vaccine Especially good results have been claimed for colon bacillus vaccine in urticaria Foreign protein is beneficial in the treatment of anthrax and erysipelas

Diseases of eyes Non specific therapy in the form of boiled milk or typhoid vaccine has been employed extensively in iritis, uveitis, keratitis, conjunctivitis and other inflammatory conditions of the eye Key (1924) produced experimental ulcers on the cornea of rabbits and obtained prompt relief with diphtheria antitoxin Scarlett (1927) found horse serum just as satisfactory as diphtheria antitoxin He considers protein therapy a "valuable adjunct" in the treatment of ocular infections, but always in conjunction with regular routine treatment

Gynaecology In pelvic disease the most important field of protein therapy has been in adnexal infections of an acute and subacute type Its chief function is in the relief of pain and extreme tenderness Stuhler (1935) of the Mayo clinic has found foreign protein therapy a good measure in pelvic cellulitis and in acute as well as chronic salpingitis In his experience it is especially adapted to more cases in which pus formation has not yet started In his opinion it is the method of choice in cases in which surgery is not yet indicated or is contra-indicated He believes that protein therapy has saved a great many patients from major surgical operations

Genito-urinary infections Gonorrhoea and its complications have been treated by various forms of non-specific therapy

as well as by gonococcus vaccine. Particularly good results have been reported in epididymitis and in gonorrheal arthritis.

Peptic ulcer It has been tried with some relief in pain of the ulcer. In view of the marked tendency of ulcers to periodic remissions and exacerbations, the result of protein therapy in such conditions must be accepted with considerable reservations.

Vascular diseases One of the newer fields for foreign protein therapy is that of vascular diseases, particularly thrombo-angitis obliterans. In vascular disease, however, it is probably vasodilatation rather than the fever, leukocytosis or mobilization of immune bodies that is responsible for the beneficial effects obtained. Fever therapy produces release of spasm of the partially occluded vessel with resulting increase in local capillary circulation. This is followed by cessation of pain and healing of ulceration, if they exist. Besides thromboangitis obliterans, fever therapy is used with some success in Raynaud's disease. The danger of thrombosis as a complication of treatment should be kept in mind.

Allergic Diseases In 1909 Biedl and Kraus found that an animal sensitized to a foreign protein could be partially desensitized with peptone and this work has been confirmed by other investigators. No doubt this explains the beneficial effects sometimes obtained by protein therapy in such conditions as asthma, hay fever, urticaria.

Contra-indications The more important contra-indications to intravenous foreign protein therapy are —

- 1 Advanced, arterial, renal or cardiac disease. Patients with cardiac decompensation should not have intravenous protein therapy. On the other hand, rheumatic endocarditis with good compensation is not a contra-indication.
- 2 Allergic states or conditions of marked protein sensitivity such as angioneurotic oedema, giant urticaria and the like.
- 3 States of extreme exhaustion following prolonged illness.
- 4 Pulmonary tuberculosis, active or quiescent.

- 5 Haemorrhagic conditions such as haemophilia, bleeding ulcers and the like
- 6 Chronic alcoholism for fear of delirium tremens
- 7 Marked nervous sensibility such as that seen in hyperthyroidism and the like

The contra-indications for subcutaneous or intramuscular injections of protein are much less stringent than for intravenous injections. Indeed, there are very few who cannot take with immunity small doses of bacterial vaccine, boiled milk or serum subcutaneously.

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Case Reports

LEUKEMOID BLOOD PICTURE IN A CASE OF LOBAR PNEUMONIA

By

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The following case of lobar pneumonia presents features sufficiently unusual to warrant publication

CASE REPORT S J, a Hindu male, aged 22, was admitted to the medical wards of the K E M Hospital, Bombay, on 17th, January 1942, with a five days' history of continuous high fever, cough with expectoration and pain in the left side of the chest. On examination (17-1-42), the patient was seen to be a fairly well-built young man with a sallow complexion and pale mucous membranes. There was definite limitation of movement on the left side of the chest, with increase of vocal fremitus and resonance, the left side was dull on percussion while auscultation disclosed the presence of crepitations on that side. There was no apparent increase in size of the liver, spleen or lymph-glands. Fluoroscopic examination of the chest was rewarded by the finding of "an extensive area of pneumonic consolidation on the left side of the chest." The temperature came down to normal within 24 hours of admission (on the 6th day of illness).

A blood count (19-1-42) showed a marked degree of leucocytosis with the presence of large numbers of "parent cells" (See Table)

A second blood count (27-1-42) a week after the first showed a perfectly normal blood picture (See Table)

Fluoroscopic examination of the chest (on 2-2-42) showed a total disappearance of the lung opacity. The patient, free of symptoms and signs, was discharged from hospital a couple of days later.

DISCUSSION High leucocyte counts with preponderance of immature or "parent" cells, have been reported from time to time in association with various pathological conditions. Because of their superficial resemblance to true Leukaemias, these benign and evanescent blood-reactions have been described as "Leukemoid states" (Krumbhaar, 1926) or as "secondary or symptomatic leukaemia" (Ward 1913).

Leukemoid reactions of the blood have been described in a variety of disorders eg tuberculosis, variola, varicella, pertussis, glandular fever, Vincent's angina, agranulocytosis, syphilis, suppurative states, neoplastic diseases, lymphadenoma, otosclerosis, mustard gas effects poisoning from mercurial ointment etc (For a complete review of these conditions, consult Forkner's monograph on Leukaemias)²

TABLE, showing blood examination reports

Description	10 1-42	27 1-42
R B C Count	1,020,000	1,060,000
Hb. %	28.8%	37.5%
Colour index	0.70	1.0
W B C Count	75,400	8,950
Polymorphs	51%	70%
Lymphocytes	10%	29%
Eosinophils	2%	1%
Mononuclears	0%	0%
Basophils	2%	0%
Myeloblasts	1.5%	0%
Metamyelocytes	0%	0%
Myelocytes	18.5%	0%
Eosinophilic	1.5%	0%
Basophilic	2.0%	0%
Neutrophilic	13%	0%
Normoblasts	1 air number	Occasional

Leukemoid reactions have been reported in lobar and other forms of pneumonia by various authors. In Osler's case (1892)⁴ of pneumonia, there were 114,000 white cells per cmm, in Laehr's case (1893)³ there were 115,800, in Turk's case (1898)⁷ there were 115,000, in Steven's case (1902)⁶ of bronchopneumonia there were 236,000 and in Austrian's case (1911)¹ there were 105,000 white cells. In the present case, there were 75,000 total whites with a preponderance of immature cells.

An unusual feature about the present case is that the high leucocyte count was noted actually more than 24 hours after the crisis, this is not in accordance with the findings of Piney (1928)⁵, in the opinion of this author "the total number of leucocytes falls suddenly at the time of crisis", "at the true crisis the total leucocytes may fall to normal or even lower, while the neutrophils gradually return to normal percentage proportions."

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Analytical Review

PREVENTION OF DIABETES MELLITUS

By

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(Continued from p 395)

In old people it is undesirable suddenly to bring down the sugar. Many feel better with a permanently raised sugar and the danger of over dieting even in the presence of glycosuria must be kept in mind.

Patent diabetic foods

Before closing the subject of diet, a warning should be uttered against the use of patent diabetic foods offered on the market, because (1) Except in the case of manufacturers of high repute, the claims in most instances are by no means invariably accurate and may be actually misleading, (2) Protein contents of many of these foods are high and are likely to be disregarded by the patients. They give a false sense of security and the patient under a belief that they are harmless may eat large quantities. Thus a large excess of protein over and above the calculated quantity of carbohydrate may be consumed. It is, therefore, much better that a patient should confine to ordinary foods of known values, which also have the advantage of being much cheaper than the patent foods.

Man is one of the few animals with widely varying appetites, fads and fancies. He possesses idiosyncrasies to many kinds of food as is aptly said "one man's food may be another man's poison". Prescribing of a diabetic diet is often a difficult and sometimes a thankless task and should not be undertaken by any one who is not familiar with the subject of nutrition and dietetics.

Summary

If a mild diabetic is to preserve his health and vigour and to prevent himself from becoming worse and to guard against dangerous complications, his diet should be such as,

(1) Would maintain him slightly below his normal body weight. Such a diet should therefore be 10 to 15% less in caloric value than that of a normal person of the same age and weight, but it must be sufficient to meet his nutritive requirements. This is

made possible, because of the ability of man to gradually adjust himself to a somewhat lower nutritive level, through a process of slight under-nutrition. Reduction, however, cannot be made beyond a certain level at which starvation begins and a complete break down in health results.

(2) Would prevent those abnormalities that lead to the increased production of ketone bodies resulting in acidosis and coma. This is obtained by giving restricted amount of fat with enough carbohydrate to ensure its complete combustion.

(3) Would control metabolic process in such a manner as to promote improvement in the ability of the tissues to utilize carbohydrate. This is done by giving carbohydrate with or without Insulin in quantities which would maintain an optimal blood sugar level (bet 0.1% to 0.16%) necessary for the proper secretion of Insulin.

In pre-insulin days it was difficult or rather impossible to achieve each of these objects but to-day, thanks to Banting and his colleagues, it is possible to do so, at least to a point calculated to be theoretically accurate.

INSULIN

Next to diet, Insulin is the most important adjunct in the treatment of diabetes. Its importance as a therapeutic agent has been thoroughly established but there still appears to be some difference of opinion as to when it should be used. It is true that a great many patients suffering from mild diabetes can do quite well on simple dietary restrictions and do not require the use of Insulin. Very recently Fetter, Durkin and Drinker, have observed that mild cases of diabetes usually seen in middle aged, obese persons can be controlled by reducing and maintaining their weights at the ideally normal level for their height, age and size, without use of Insulin (Am Jour Med Science June 1938).

He recommends the use of Insulin as an initial measure in diabetes irrespective of the degree of its severity. He advocates the early use of Insulin, though not always a necessity, the establishment of a maintenance diet and earlier attention to health and should prove a valuable occasion to use it at a later date.

about the immediate use of Insulin

(1) In all cases of coma in which ketosis is present in large and repeated doses, (2) in cases of acidosis. The subjects with any degree of ketosis should receive Insulin.

against danger-

optimal blood
sugar level
in color

1. Fetter, M., B.
2. Osler, W., "I
3. Pines, A., "Re
4. Stevens, J. L., "I
5. Turk, W., Kinsch

treat glycosuria by restricting the diet will inevitably increase the formation of acetone bodies, (3) In all children in whom Insulin is always indicated for two reasons (i) the diabetes is usually severe and runs a rapid course, (ii) there is a greater need for comparatively large amount of food on account of their growth and development and their great activity, (4) In pregnancy, glycosuria can seldom be controlled without the use of Insulin, (5) In cases of gangrene or severe infections, Insulin must be given from the very start in comparatively large doses till sepsis has cleared up, (6) In cases which require surgical operation, Insulin and glucose in large doses must be given in order to protect the liver cells against damage caused by the anaesthetics, (7) In all cases where the urine contain 2% or more of sugar as shown by the turning of Benedict's solution yellow by a few drops of urine (Joslin) or where the fasting blood sugar is found to be over 0.2% (Graefe) Such cases are regarded to be very difficult to control by diet alone

All are agreed as to the imperative need of Insulin in patients whose urine cannot be rendered sugar-free on diet absolutely required to maintain their weight and vigour, but the difficult question arises in border-line cases in which the diet which they can take and still be sugar-free, is low enough to keep them fit and active. It is much better to allow such patients to take a fuller diet and feel well and avoid future complications with the help of Insulin rather than to allow them to struggle on without it, and remain under-nourished but sugar-free

The main objections against the use of Insulin are pain and inconvenience to the patient caused by injections which are as a necessity to be taken often more than once in a day. Cost is also a consideration in the case of some patients. As Insulin is taken before meals and two or three times a day, it may not be possible for the doctor to attend and give the required Insulin injections. Hence, the patient or some member of the family who can understand the use of Insulin must be taught the use of syringe in the administration of Insulin injections. Insulin dosage and its adjustment to suit the various needs of the patient are matters to be decided by the doctor treating the case and beyond the scope of the present article.

Most people still look upon Insulin as an habit forming drug and to cause addiction. This erroneous notion combined with exaggerated fears, hypoglycemic reactions, prevents many people from submitting to Insulin treatment. It is unfortunate that inspite of its being introduced into medicine as far back as nearly 15 years, Insulin is looked upon as a last hope and not the first line of treatment as it ought to have been. Its beneficial effects are many and outweigh the minor inconveniences attending its administration. Fortunately the recent discovery of a new compound in the form of Zinc Insulin Protamate by the Danish worker Hagedorn has greatly done away

with the necessity of giving injections several times a day. It is not easily destroyed in the body and its action lasts for a longer time than Insulin proper.

However, it must be distinctly understood that Insulin does not do away with the necessity of strict dietary control, but on the other hand has made it more imperative and more difficult. It is the exact balance between Insulin and the appropriate diet on which depends the success of diabetic treatment, though exercise also plays some part.

Insulin may cause unpleasant and rarely fearful symptoms, due to hypoglycaemia brought about by an overdose or to lack of sufficient carbohydrate being taken after Insulin injection. Patients should be instructed to be careful on the look out and recognize the early symptoms and to take sufficient quantity of easily assimilable carbohydrate such as a lump of sugar, syrup, or fruit juice.

EXERCISE

Properly regulated exercise has an important place in the treatment of diabetes. It has been assumed that exercise specifically stimulates Insulin secretion and it leads to better oxidation of carbohydrate, so that the usual rise in the blood sugar curve is not obtained when the dextrose tolerance test is carried out during or after exercise, (Hale, White & Payne, Strandell—1925). It may be that exercise by developing the muscles tends to increase their storage capacity for glycogen. It has been known even before Insulin was discovered that in mild diabetes, exercise is always beneficial in reducing the sugar in the blood, as the latter is burnt up by using the Insulin to its utmost capacity. It has often been found that after exercise, sugar from the urine entirely disappears and more food can be taken without producing glycosuria. On the other hand in severe cases of diabetes in which Insulin production is almost nil, exercise without Insulin is harmful. The patient gets exhausted, and is rendered hypoglycaemic owing to the depletion of already deficient glycogen store in the liver. However, with the help of Insulin, walking, Swedish exercise and mild games can be indulged in with great benefit. There is one important point which should be noted with regard to exercise in cases treated with Insulin, that is, it may cause Insulin reaction. If a diabetic in whom an equilibrium is established between a certain diet and a correct dose of Insulin, an unusual amount of exercise by burning up more sugar than otherwise may reduce the sugar in the blood. Hence exercise must always be taken into account when administering Insulin, for, other things being equal, with greater amount of exercise Insulin will be needed in a smaller dose. Children are very susceptible to exercise and require either extra carbohydrate or an equivalent reduction in the Insulin dosage whenever they indulge in strenuous exercise or

game On the other hand, if an Insulin case has not the usual exercise as for instance when he is confined to bed for any reason, more Insulin is needed to control the urine sugar, because the muscles do not help to remove the sugar from the blood On resuming exercise, the dose of Insulin requires to be proportionately decreased

Soskin (1934), however, has observed in two patients that there was no worth noting decrease in the Insulin requirement during the time they underwent a systematic course in physical training

General Diabetic Hygiene

The diabetic patient should strive to lead a regular and well ordered life in strict conformity with the laws of personal hygiene Besides regular exercise, he must take sufficient sleep and rest, avoiding undue mental and bodily fatigue A rest of about one hour may, if possible, be taken in the middle of the day

Mental peace and freedom from emotional disturbances are absolutely essential for the well-being of the patient and to prevent serious upsets in the smooth and mild running of the disease He should, therefore, always preserve coolness and equanimity of mind

He must always be careful to preserve the regularity of his bowels by providing enough roughage in the diet, by taking plenty of leafy and green (3%) vegetables Equally necessary it is for him to avoid diarrhoea and stomach upsets by carefully selecting food which must be simple and easily digestible He must devote a certain amount of time after the cleanliness of his teeth and skin which is prone to many kinds of disease Teeth should be brushed after every meal and at bed time If pyorrhoea or a diseased tooth exists, a dentist should be consulted If removal of tooth is deemed necessary, it should be done with the co-operation of the family doctor and the dentist

Similarly, great care should be taken to avoid infection, even common cold and cough, and also injuries A diabetic patient should never be in a hurry, as for instance to catch a train or a tram or in going down the stairs, in order to avoid accidents and thereby injuries which exert most baneful effects on the diabetic Bruises and cuts such as might easily result from paring nails or cutting corns and callosities must be early attended to On the first sign of any inflammation of the skin such as redness, pain etc, and in all cases of injury, the diabetic patient should seek medical advice

Certain diseased conditions such as pyorrhoea, infected tonsils, boils and carbuncles are known to greatly lower the sugar tolerance, and therefore should be immediately treated Gall-bladder, and appendix, if diseased must immediately be attended to and during the quiescent period of the attack should be operated upon and removed

In short, the diabetic should realize his handicap and take cheerful view of his condition, for it is known that under proper care and treatment a *diabetic seldom dies of diabetes*. On the other hand, it is the complications which usually carry the patient away and therefore they are to be vigilantly watched for and treated on the appearance of their earliest signs.

COMPLICATIONS AND THEIR PREVENTION

Since the advent of Insulin it has been found possible, with a little care and effort to ward off many of the complications from which diabetics are prone to suffer, as they usually set in very slowly and are preceded by a set of easily recognizable symptoms. It is known that as long as urine is kept free from sugar and acetone bodies, there are very few chances of complications setting in, if at all, very suddenly. The duty of the doctor is therefore twofold, viz (1) to make frequent urine examination to detect sugar and especially acetone bodies and (2) to apply such measures as would keep the patient's urine free from sugar and acetone, and institute prompt and appropriate treatment on the appearance of the earliest symptoms.

Fortunately, in the case of almost all complications, there is very little difference between the prophylactic and curative treatment, except in a few minor details.

Complications commonly seen in diabetics, usually fall into three groups, viz, (1) acidosis and coma, (2) arteriosclerotic changes of the vessel walls, and (3) surgical complications including gangrene and infections.

(1) Acidosis and Coma —

Every diabetic invariably runs the danger of coma, but the risk is greatest in poorly treated or untreated cases. This usually occurs under either of the following conditions: (i) Dietetic imbalance, (ii) Omission of Insulin, (iii) Gastro-intestinal disturbances, (iv) Infections and (v) Trauma.

(i) *Dietetic Imbalance* —An improper diet especially of a high caloric value and containing fat in amount much greater than the carbohydrate can completely burn, always tends to produce acidosis, due to accumulation in the blood of poisonous products of incomplete fat combustion. On the other hand, a properly balanced diet containing sufficient amount of carbohydrate to completely burn the fat is one of the greatest safeguards against acidosis and coma.

(ii) *Omission of Insulin* —Obviously, if a diabetic requires Insulin to keep his urine sugar-free on an adequate diet, he runs a great danger of acidosis, if he fails to get his Insulin unless the diet is at the same time reduced.

(iii) *Gastro-intestinal Troubles* —Dangers are of two fold nature In the presence of vomiting or diarrhoea, sufficient food may not be absorbed and if the dosage of Insulin is continued, there is a risk of hypoglycaemic reaction occurring On the other hand, there may be starvation from want of absorption of sufficient food, causing excessive breaking down of body protein and fat, which greatly favours the production of acidosis In all cases of gastro-intestinal troubles, Insulin dosage should not be omitted nor reduced, but an increase should be made in the amount of carbohydrate which should be given in the form of liquids in sufficiently large quantities Urine examinations need to be frequently made

(iv) *Infections* —If a diabetic whose urine has been kept sugar-free by proper treatment begins to show glycosuria on the same diet and the same dosage of Insulin the physician should immediately suspect and search for the presence of an infection, even if there may be no fever Infection greatly lowers the sugar tolerance of diabetic patients and renders him less sensitive to Insulin and greatly disturbs the routine treatment Extra care on the part of the patient and doctor alike is necessary even in the case of a minor infection such as common cold Urine must be tested several times a day for sugar and acetone in severe infections and on the appearance of the slightest trace of acetone, treatment for threatened coma should be immediately instituted

During an infection, Insulin requires to be given in a relatively large dosage given in small but repeated doses and continued until the infection disappears Careful supervision of the patient is specially necessary early in the convalescent period, because with the disappearance of infection, the need for additional Insulin is greatly diminished or abolished and if the same dosage of Insulin is continued, hypoglycaemic attacks are likely to occur It is advisable always to give patients suffering from pneumonia, tonsillitis, or other infections, a diet richer by 400 to 600 calories than the maintenance diet and containing a somewhat higher percentage of carbohydrate than would ordinarily be used in treating the diabetic condition (Williams and Wilkins 1925) Fat and protein contents in the diet may be reduced with advantage for the time being

Diabetic patients on the other hand are specially prone to infections of the lungs e.g pneumonia, tuberculosis, etc They should therefore always try to keep themselves in a fit condition by means of diet, exercise, fresh air and sufficient rest, and take scrupulous care of the skin On the slightest sign of ill health, they should seek medical advice and treatment

(v) *Trauma and Surgery* —Injuries either accidental or due to surgery are dangerous as they tend to produce acidosis and coma in a way which is not still exactly known To guard against acidosis,

carbohydrate in the diet should be increased and, if the patient is bed-ridden, be given in the liquid form. The total Insulin dosage will be required to be increased, and should be given in small and repeated doses.

As far as possible, diabetics, should avoid such occupations which involve more or less a certain risk of trauma or an accident.

SURGERY IN DIABETES

It presents certain difficulties of its own and requires the co-operation of the physician and the surgeon. To avoid danger, it is essentially necessary for the doctor to decide whether a surgical condition exists and to institute immediate treatment with a view to minimize the risk of infection and to fortify the patient for the added strain that surgery in the diabetic entails. In all cases, hospitalization of the patient is much to be preferred.

Gangrene, carbuncles, furuncles and abscesses are the main conditions in the diabetic that demand prompt surgical intervention. It must be remembered that a clean unbroken skin is a great protection against the necessity of surgery.

The choice of the anaesthetic and the technique of the operation are purely surgical matters and must be decided by the operating surgeon, but usually the care of the patient before and after the operation remains in the hands of the general practitioner.

(1) Pre-operative care—Diabetics requiring surgery may be divided into two groups according to the length of time available for the preparation of the patient. It is extremely desirable that the primary condition—diabetes should be under control so that the patient is able to take an adequate diet and his urine is free from sugar and acetone.

(a) Preparation of the elective cases—If there is no need for haste the patient should be made free from glycosuria and from acetone bodies, if they are already present, by means of Insulin and a properly balanced diet. S. Standard (P 627 JAMA 26 Feb 1938) recommends a high carbohydrate—limited fat diet consisting of 180 to 250 gms carbohydrate, 70 to 80 gms protein, and 75 to 85 gms fat, to be given several days before operation.

Just before the operation, to guard against dehydration liquids in the form of orange juice (300 cc) or glucose solution should be given by mouth, 1 to 1½ hours before the operation. In severe cases particularly in abdominal cases in which vomiting is an important feature, more than 1,000 cc of normal saline containing 6% glucose should be administered intravenously. If necessary from 4,000 to 5,000 cc may be given during the 24 hours (S. Standard 1937).

Frequent urine analysis would determine the dosage of Insulin which is comparatively large and is given in small but repeated doses. It would be preferable to estimate the "CO₂ combining power of the plasma" before operation and if found less than 40 volumes per cent additional glucose and Insulin may have to be given.

(b) Preparation of emergency cases—In the presence of an infection, urgent surgery should not be delayed. If the patient is not under diabetic control, and the operation is of an emergency nature, the treatment should be on the lines of that of acidosis with threatened coma.

(u) Post operative care —Transient glycosuria is a frequent occurrence after operation. Nevertheless liquid carbohydrate feeding should be started about 3 to 4 hours after the operation. The patient should receive the usual amount of carbohydrate allowed to him before operation, in the form of liquids with adequate doses of Insulin. In from four to six days the patient is returned to his regular diet in a semi-solid form divided into 4 or 5 feedings. Whilst within 10 days if his condition permits, the patient is put on three meals a day. During recovery, attention will have to be paid to the Insulin requirement of the patient which is often changing and also to the diet at the same time.

(2) Arteriosclerosis —

The incidence of arteriosclerotic changes varies directly with the age of the patient. When not present at the onset, it develops earlier in diabetes than in non-diabetic persons. Arteriosclerotic changes are believed to be associated with a diet rich in fat which causes hypercholesteræmia. It has been observed that on properly balanced and specially high carbohydrate—low fat diet, a definite drop occurs in the cholesterol content of the blood and that it is possible at least to delay the occurrence of arteriosclerotic changes. Sanson advocates an alkaline residue diet with a liberal allowance of carbohydrate.

Of all the serious consequences of arteriosclerotic changes in the case of a diabetic, the most painful and sorrowful is a gangrene of the lower extremities.

(3) Gangrene —

It is very common in the old but rare in young, just the opposite to coma. As a precaution against gangrene one must be ever watchful for early signs of impaired circulation in the extremities, such as claudication, coldness, pain, diminished arterial pulsation, rose spots, blots, and blisters. At the same time utmost cleanliness of the body must be insisted upon, particularly of the feet. Trauma

and local infection need be immediately attended to. Measures to improve the circulation such as Buerger passive exercises in the raising and lowering of the feet, massage and warm foot bath are of much value. Tight-fitting footwear, garters, belts and other constricting articles of clothing should be strictly avoided.

Other methods of exercise such as recommended by Hermann and Read, and by Landis and special apparatus for securing hyperaemia of the parts have been devised, but have not been found useful. Jacobi recommends intravenous administration of 2% sodium Iodide in normal saline which is believed to reduce the amount of iodine in the blood.

In importance to gangrene, complications from arterio-sclerotic changes are (1) Sclerosis of the coronary arteries leading to myocardial weakness and coronary thrombosis (2) Retinitis (3) Sclerotic changes in the kidneys (4) cerebral thrombosis and haemorrhages. Prevention of these complications lies in the general treatment of diabetes which are calculated to prevent or delay the arterio-sclerotic changes in the body (5) Neuritic pains — Diabetics often complain of pains in the legs due to neuritis which at one time was believed to be caused by hyperglycaemia. Now, neuritis is believed to be due to vitamin B1 deficiency and is treated by means of vitamin B concentrates.

DIABETES IN PREGNANCY

It is rather dangerous for a woman to marry and become pregnant, because of parturition. Many women do not become pregnant or if they do, they usually abort. Toxoemia, eclampsia and still birth occur more frequently in diabetic women than in non-diabetic. There may be also failure of lactation. During pregnancy, sugar tolerance is liable to change from time to time and after delivery it may or may not return to normal. Frequent urine examinations during pregnancy are absolutely necessary in order to make proper dietary and Insulin adjustments. The treatment of a pregnant diabetic woman is practically the same as of a non-pregnant woman, but she must receive a relatively full diet, composed mainly of proteinaceous foods viz milk, eggs, green vegetables, fruits, fish and meat. Diabetic women bear usually large babies. Duncan advises therefore a restricted diet at least during the last three weeks of pregnancy. P. White and Randall, (36 Mayo clinic) advise premature labour or a caesarean section to be performed 2 or 3 weeks before the calculated date of delivery to avoid the risk of a difficult labour, the risk of asphyxia and maternal death due to ketoacidosis. Insulin, and from diminished sugar in the blood, be remembered that a child is born with diabetes. Cases of congenital diabetes.

DIABETES IN CHILDREN

Diabetes in children runs a rapid course and before Insulin came into use, diabetic children usually succumbed to coma or an intercurrent infection within a relatively short time after the onset of the disease. Today with Insulin, the diabetic child can certainly hope not only to live long, but to grow and become a useful citizen. Inadequate treatment if it does not result in coma, always means pseudo-dwarfism or chronic invalidism and illness at a later age. Heredity, pituitary overactivity and infections are believed to be most important factors in juvenile diabetes.

The essentials of treatment in children for all practical purposes are the same as those in the adults, but to treat a child requires great tact, resourcefulness and patience on the part of the parents and the doctor, together with a careful and constant watch for an unexpected complication suddenly setting in. As regards diet it must not be copious as to favour obesity, but it must be sufficient for the normal growth of the child. Diet with a caloric value 50% above the basal requirement is found quite satisfactory. The following are the caloric requirements of diabetic children according to age: (1) between 1 and 5 years, 1,000 to 1,400 calories, (2) between 5 to 10 years, 1400 to 1800 calories, (3) between 10 to 15 years, 1,800 to 2,000 calories, and (4) between 15 to 20 years 2,000 to 2,500 calories, (Joslin).

The diet must contain sufficient quantities of animal protein and protective foods such as milk, eggs, and fruits as to provide enough vitamins and essential minerals especially calcium and phosphorous. Protein allowance must be liberal ranging from 35 gm per kilo body weight in a child 1—3 years old to 2 gms per kilo body weight in a boy 15-17 years old. Experience has shown that best results are obtained when carbohydrate in the child's diet is at least double the quantity of fat. The present day tendency is to give carbohydrate in still larger amount with proportionately greater Insulin doses. In children diet remains stationary, whilst Insulin and exercise vary. Insulin must be given in sufficient quantity to keep the child on an adequate diet and free from sugar. It is better to give in small and split doses as many children are sensitive to Insulin. Children must be encouraged to take part in out-door exercise and games which are not very strenuous as exercise reduces the Insulin dose.

Diabetic children run a greater risk of acidosis and coma than grown up persons as they are susceptible just like normal children, perhaps more to eruptive fevers, infections of the respiratory tract and dietary indiscretions.

ADJUNCT CURES

Finally, a brief reference may be made to several methods of cures which have been proposed during comparatively recent years.

by a few enthusiastic observers as useful adjuncts in the treatment of diabetes

(1) Fasting —Allen in 1913 observed and emphasized the beneficial effects of fasting. From that time onwards till the discovery of Insulin (1913-1922), short fasts were almost always prescribed just before putting the patient on diet. Short fasts have been shown, in animals by Abderhalden and Lambe and in man by Folin and Denis, to be safe and effective and therefore may be prescribed periodically in mild cases with advantage. On such days, fruits and vegetables of a small caloric value may be given. On the other hand in severe cases of diabetes, fasting is very dangerous because of the great risk of acidosis being produced by the sudden withdrawal of food.

(2) Liver Diet —On the assumption that liver is often affected in diabetes, liver and liver extracts have been used in the diabetic treatment. L. Pinnel (1937) has on the other hand observed actual hyperglycaemia being produced by injecting liver extracts.

(3) Incretine —La Barre found that incretine (an extract of the duodenum) would keep depancreatized dog alive. He has recommended it as a method of treatment for diabetics.

(4) Succinic acid —Szent-Gyori has suggested the use of Succinic acid orally in the treatment of diabetic acidosis (Lancet P 200, 24 July 1937).

(5) Oral preparations used as substitutes or aids to Insulin—Several preparations mostly containing drugs such as opium or its alkaloid Codeine and synthetic drugs like synthalin, mytilin, (Ivy), Decholin, etc., have been put on the market and are prescribed by doctors as substitutes for Insulin. Such preparations have not only been found useless but in some cases to produce actual harm, besides giving a false sense of security to the patients. Extracts of organs and specially of the raw pancreas have been similarly pushed in the market by several manufacturers. But all of them have been found to be useless.

(i) Opium —Lanfheldt (Norway) believed that opium lessens glycosuria by reducing or depressing the secretion of Adrenaline (Lancet P 1135, 13 Nov '37), on the other hand Bodo, Cotui and Benaglia (1937) have found slight hyperglycaemia being consistently produced by morphine in animals after Adrenal inactivation (Jour Pharm & Exp Therapeut Jan 1938).

(ii) Synthalin is often used in combination with decholin in the treatment of diabetes mellitus with a view to replace Insulin. They are known to reduce sugar in the urine through their action on the kidneys and liver, which are, however, known to be injured by these drugs when used for a long time.

(iii) Copper sulphate in pills (Schnetz) and sulphur have been suggested

(6) Ultra Violet Rays —L. Pincussen has found that Ultra Violet rays influence carbohydrate metabolism just like Insulin and lower the level of blood sugar with an increase in the glycogen content of the liver and muscles (B M J p 64—16 April, 1938) Humphries (Artificial sunlight and its therap 1929) whilst admitting the value of ultra violet rays cautions against their indiscriminate use, because of the risk of increased metabolism and acidosis

(7) Surgery —Since the time (1907) Zuelzer proposed the theory that adrenals have an important part in the development of diabetes, various procedures both surgical such as cutting of the splanchnic nerves, resection of the sympathetic ganglia or partial destruction of the medulla and roentgenological such as irradiation of the adrenal region, have been employed with a view to suppress the medullary secretion. The results have not been found encouraging and a few fatalities have been known to occur after operations. Very recently Rogoff, Ferrel and Nixon have shown that during the diabetic state produced artificially by the total removal of the pancreas there is an actual reduction in the adrenal medullary activity (J.A.M.A. Editorial P 655 26th Feb 1938)

(8) In very recent years experiments are being carried out to test the efficacy of Insulin by determining its absorption when introduced through the nasal mucous membrane and through the skin. The results are being awaited with much interest.

(9) Diets —In the past, before the advent of Insulin, in every country at one time or other, many systems of diet such as Von Noorden's oatmeal cure, Donkin's milk cure, Mosse's potato cure, During's rice cure, etc., were tried with claims of success by their respective authors. But none of them was found to be satisfactory and to survive for a long time.

EPILOGUE

Insulin together with the changes made on rational basis in the diabetic diet during the past few years has brought about very encouraging results which are reflected not only in the diminished diabetic mortality but also in an increase in the expectation of life at all ages, but specially the young (eg by 30 years at the age of 10) and among both sexes (Joslin—Mortality and Longevity of Diabetes, Ame Jour Med Sc May 1938). But still, no case of diabetes has ever been known to be cured radically beyond doubt and also the death rates of diabetics are much in excess of those for the general population. Moreover, it is not uncommon to come across cases of Insulin resistance which have been recorded in not too small a number since Insulin first came to be used in the treatment of diabetes in 1923 and for which no explanation is still forthcoming. To

quote an instance, a case of severe Insulin resistance was recently observed by Alexander Glen et al in a female patient who received 900 and later 1050 units of Insulin per day during a period of 27 days without any appreciable effect on the blood sugar or glycosuria (Quart Jour Med P 271, April 1938)

Under such circumstances the present method of diabetic treatment at its best cannot be said to be perfect and without fault or reproach, and would require to be much improved upon or totally altered before it can be expected to bring about a radical cure

Considering the rapid advances made in recent years in our knowledge of the physio-pathology of diabetes, and the intensive researches that are being carried out at present in almost all important countries over the world, it is not unlikely that one day, a startling discovery would be made which may change all previous ideas about diabetes and turn the possibility of prevention as well as cure into a reality. How many years it will take to achieve, it is impossible to say. Much depends upon the money and labour spent on researches which only are to be depended upon for the final solution of all problems of diabetes including its prevention.

Fortunately, however, the etiological factors which have already been considered carry many possibilities, if not of completely preventing or stamping out diabetes from the community, at least of greatly reducing the incidence and mortality of the disease, provided a concerted effort on the part of every one concerned, is made in the right direction. A close co-operation between the laboratory, hospital, and the general practitioner would be greatly necessary, in the successful fight against the disease.

At present, the only sure method of preventing or controlling the incidence of diabetes is by way of (1) avoiding hereditary transmission of the disease by restricting marriages between two known diabetics or diabetes carriers, and (2) recognizing under nutrition as a powerful aid in the prevention or postponement of diabetes and a foundation stone of diabetic treatment and insisting upon normal weight or slight underweight in a diabetic, suspected diabetic or relative of a diabetic (Joslin). For prevention of complications from which the diabetics usually die, attention must be directed towards early detection of obscure or latent cases with a view to provide treatment before any serious harm is done to the patient. This can only be achieved through a systematic and routine examination of urine of all obese persons who are over thirty but particularly of those who have diabetic relatives, at least once every year.

In all cases it is essentially necessary to secure the intelligent and wholehearted co-operation of the patient without which any form of treatment is bound to fail. He must be explained carefully

the physio-pathology of diabetes and must be impressed of the great risks entailed in neglecting the disease and also of the advantages resulting in good health, comfort and long life by adhering to a carefully planned treatment which at present consists in the judicious combination of DIET, INSULIN, and EXERCISE

It is hoped that when the public takes itself to the scientific way of preventing or arresting the disease, it will not be a great many years before diabetes mellitus becomes a rare disease and ceases to be a serious health menace

Critical Notes and Abstracts

THERAPEUTIC NARCOSIS

I *SOMNIFAINE NARCOSIS* J Kearney and P J Courtney record (Journ of Mental Science, Jan 1938) the results of 40 treatments in 38 cases of mental disease. The technique employed has been that recommended by Strom-Olsen. Those about to undergo treatment were put to bed in a quiet, darkened room, under constant observation. McCowan (1936) and Hennelly (1936) have pointed out that under these conditions the effective dose is much smaller than would otherwise be necessary, and we agree with this view. Menzies (1937), however, carried out his treatments in an open ward.

From this it will be noted that in 75% of the cases the total quantity of somnifaine administered to each patient in twenty-four hours did not exceed 4 cc.

Somnifaine was injected intramuscularly at 9 a.m. and 6 p.m., except in one case, in which large doses were necessary, and the time of injection depended on the reaction. Insulin, 10 units twice daily, and glucose, 1 to 1½ oz. three times daily, were given throughout the course of the treatment, as recommended by Strom-Olsen and Quastel, although this method has recently been discounted by Menzies (1937) and Palmer (1937). Some cases who became restless during the night were given 2 drms of paraldehyde, and this was sufficient to maintain narcosis until the morning injection was due. The patients sat in an upright position for meals, thus minimizing the dangers of aspirating food. They were also supported on a commode, when attending to personal needs, in order to counteract any danger of pulmonary congestion from prolonged recumbency. The diet was entirely fluid. A certain degree of dysphagia is always present, and the giving of a solid or semi-solid diet is dangerous, owing to the risk of choking, and aspiration pneumonia. Also the maintenance of a good diuresis is very important, and is helped by an abundant fluid intake.

It was found that the patients could be roused for meals without the slightest difficulty, and the majority returned to sleep within ten or fifteen minutes after receiving all necessary attention. A few cases required 1 to 2 drms paraldehyde to overcome occasional restlessness arising after the midday meal.

The duration of treatment was from twelve to fourteen days in all except 3 cases.

The following complications occurred in the course of our treatments. Pyrexia occurred in 21 cases, the temperature ranging be-

tween 99° and 104°F In 15 of these, as the temperature did not exceed 100°F, it was not necessary to interrupt treatment In 4 cases, with a rise above 100° F, the temperature fell to normal on withholding the drug for twenty-four hours One case developed a temperature of 104°F, with albuminuria and symptoms of circulatory collapse on the fourth day, and the treatment was discontinued

Symptoms of circulatory collapse appeared in 2 cases, one the case just referred to under pyrexia, and the other a woman, aged 66, who on the seventh day of treatment exhibited marked pallor, with feeble rapid pulse

Vomiting occurred in 2 cases, but was not very severe, and did not necessitate interruption of treatment

Renal Complications—Albuminuria occurred in 1 case, already referred to under pyrexia Retention occurred in 5 cases, 4 necessitating catheterization on a few occasions, and 1 throughout the entire course of treatment

Disturbances of co-ordination—Speech, in all cases, resembled that met with in alcoholic intoxication, and was apparent when the patients were well under the effects of the drug, usually on the second or third day

Ataxia was also observed, and did not disappear in 1 case for some weeks Dysphagia has already been referred to

Epileptiform convulsions—An epileptiform seizure occurred in 1 case on the fourth day after the termination of treatment There was no previous history of epilepsy

Classification of cases treated The 38 patients who underwent somnifaine narcosis, comprised 14 males and 24 females A second course of treatment was given to two females There were 16 cases of manicdepressive psychosis—7 cases of mania and 9 cases of melancholia—21 cases of schizophrenia and 1 case of paraphernia

Results of treatment		Melancholia	
Recovered	8	Recovered	2
Improved	11	Improved	2
Not improved	19	Not improved	5
Classification of Results		Schizophrenia	
Mania			
Recovered	3	Recovered	3
Improved	3	Improved	6
Not improved	1	Not improved	12

Case 3—Female, aged 34, mania Previous attack, lasting six months, occurred three years ago Admitted April 29, 1937, and somnifaine given for fourteen days, commencing on May 11, 1937 After treatment she appeared quite normal, remaining so for ten days, and then relapsed Second course of treatment given on June 7, 1937, and on its termination she was again perfectly normal, and remained so until discharged one month later

Case 5—Male, aged 48, melancholia agitata Admitted on May 28, 1937, in an extremely agitated and depressed state History disclosed that the illness was of one week's duration, and that a very determined attempt at suicide was made just prior to admission Somnifaine was given and it was necessary to increase the dose upto 8 cc daily, plus 2-3 dm paraldehyde during the night, to maintain narcosis He suffered from retention of urine throughout the course of the treatment, and was catheterized regularly Artificial feeding had to be resorted to during the first two days The treatment was continued for sixteen days, and a wonderful improvement was evident on the seventeenth day This improvement continued, and he was discharged two weeks later

Case 11—Female, aged 22, schizophrenia Admitted on September 22, 1937, in a state of catatonic excitement She was given a course of somnifaine, beginning on the day after her admission, and there was no change in her mental condition on completion of treatment Four days later an epileptiform convulsion occurred, and this was followed by a very striking improvement in her mental state The restlessness and excitement passed off, and the improvement is being maintained

Summary 38 cases were treated by prolonged narcosis with somnifaine, 21% recovered, 29% improved and 50% were unchanged

It might be well to mention here the opinion of Meeloo that the original dosage of 8-12 cc somnifaine per day has been reduced in the course of time to 2-4 cc per day, with a corresponding reduction in the number of successful treatments Kiasi, using large doses, claimed 16 successes from 23 schizophrenics treated, i.e., 70%

II MEDINAL-LUMINAL PROLONGED NARCOSIS Wilson and Gilman (J Ment Science, Nov 1938) discuss the use of medinal and luminal in producing therapeutic narcosis A mixture containing medinal 5 gr and luminal 1 gr in each drachm is used The first dose is 2 drm, which is repeated 4-hourly till sleep occurs, thereafter 1 drm is given as required The usual methods of nursing are adopted and Day claimed that narcosis could be continued for as long as 78 days with a gain in weight of from 5 to 30 lbs

Mania The best results were obtained in this group Of 10 recent admissions 9 women and 1 man, 7 of whom were recurrent, apparent cure was obtained in 7, 2 improved and relapsed and 1 was unchanged, but the 3 failures had 4, 5 and 9 days' treatment and the successful cases averaged 18 days The average for the whole group was 14 days, the ages were from 30 to 58 years and averaged 45.3, the average daily dose was 4.3 drm, the average loss of weight nearly 3 lbs and urine measured 31% of the fluid intake

Three chronic male patients were treated and two showed temporary improvement One of these a case with some schizoid features, has had six courses of treatment averaging 18 days each and

taking 3 drm of the mixture daily, the first narcosis produced an improvement lasting a few weeks, the second, third and fourth were valueless, the fifth again produced improvement, and the sixth has produced the best effect so far

Schizophrenia and Paraphrenia These results correspond with those of Day, who obtained improvement lasting some days only in his schizophrenics, and are not so good as those reported by Parfitt using somnifaine

Anxiety Hysteria They lost an average of 7 lbs in weight, but all showed some slight improvement, which was maintained The urine-fluid-intake ratio was 43%

Epilepsy The last case in this series was epileptic, subject to periods of prolonged excitement He was aged 30, and following 8 days of reasonably smooth narcosis without urinary changes, during which he had 28 drm of mixture, he developed an acute "barbiturate" pneumonia and died in two days Postmortem both lungs were heavily congested and pus was found in the right kidney It is striking that the only epileptic treated with somnifaine by Parfitt (4) died similarly following 12 cc of somnifaine in 3 days In both cases the patients were apparently in sound health, and although only on a basis of 2 cases, we feel justified in urging great caution when the treatment of epileptics by prolonged narcosis is contemplated

In most cases of this series we have used insulin as recommended by Strom-Oslen, and have added 10 cc of campolon given intramuscularly twice a week, but we are unable to report any striking freedom from complications

Complications Seven patients ran irregular temperatures without necessitating cessation of treatment, and 4 more developed high temperatures with signs of physical distress, which were not alarming but led to treatment being stopped In addition to these there were 3 cases of "barbiturate" pneumonia, one of which proved fatal In 4 cases treatment was abandoned because of a general impression of illness and taxaemia, and in 7 patients treatment was terminated by collapse Dysphagia was observed in 8 patients and tube-feeding was necessary in 3, but only 2 patients were troubled by vomiting in the early stages of treatment

Generalized morbilliform rashes developed in 4 cases and were treated with calcium ametox without the interruption of narcosis, and in each case the rash disappeared in a few days Retention of urine for 24 hours or longer was fairly frequent, but catheterization was only resorted to on two occasions Two patients complained of diplopia during the phase of recovery from narcosis

Two further cases had occasional pus-cells, 7 had occasional albumin and 10 had albumin regularly, the development of casts

in the urine of one of these latter led to the termination of narcosis, but otherwise the urinary findings were not taken as indications for stopping treatment. Nine cases had acetone in the urine for from one to seven times, usually during the stages of treatment.

Conclusions (1) Complications in mednial-luminal narcosis are not so frequent as in somnifaine narcosis, but the treatment presents grave dangers at times.

(2) The results of treatment are not so dramatic as those obtained by somnifaine, but on the whole are at least as good.

(3) The results in mania are excellent, in melancholia they are good, but schizophrenics do not respond to this form of therapy.

(4) In cases of anxiety hysteria showing no response to ordinary treatment initial improvement can be obtained.

(5) The treatment of epileptic psychoses is contra-indicated.

III THERAPEUTIC NARCOSIS WITH SONERYL Horsley has used soneryl (J Ment Science) to produce prolonged narcosis. The opinion at Herrison based on 40 prolonged narcosis with soneryl is that the drug is less toxic and sometimes more effective than somnifaine.

Pharmacology of Soneryl Soneryl is n-butyl-ethyl-malonylurea, a "heavy barbiturate" comparable with nembutal, amytal and dial. It is prepared in several forms to suit the varying requirements of administration. The effects are similar. Small doses in psychotics produce anomalous emotional states, with a tendency to become either confiding or lachrymose. An initial quickening of the pulse is followed by definite bradycardia. Simultaneously the blood-pressure falls by about 25 mm of mercury. The cerebro-spinal fluid pressure falls abruptly and tends to remain subnormal throughout narcosis. Over-dosage produces great depression of all vital processes. A significant and early sign of poisoning is a soft, slow pulse of about 40. This may be followed by collapse, with subnormal temperature, dilated pupils and a dusky complexion. The most effective antidote is coramine in doses of 5 or even 10 cc.

Administration and Dosage The first method of oral medication, basing the dose on body-weight, showed partial or complete failure in 10% of cases and was abandoned. The second group received the salt, sodium soneryl, by intravenous injection, and here it was considered safer and more accurate to regulate the dose by individual response, i.e., by inducing narcosis slowly and stopping the injection as unconsciousness supervened. This method never failed to induce sleep, and in single doses had no adverse effect on the circulatory or respiratory systems.

The third group received soneryl sodium by intramuscular injection. The narcotic effect was apparent in 5 or 10 minutes, and its duration equalled that due to intravenous injection. Unfortunately,

the solution is a local irritant, and 4 cases developed deep-seated injection abscesses. An alternative preparation of soneryl, in a special solvent, has been used in 20 cases without ill-effect.

These were given according to a scheme which allows for possible idiosyncrasy. This method was invariably effective and well tolerated thereby resembling the highly satisfactory results already recorded with nembutal suppositories.

The conclusion is that the intravenous and rectal methods offer the greatest therapeutic efficiency. These methods will be described separately and in detail.

I-Intravenous Therapy The immediate and profound effect of intravenous narcosis is of incomparable value in psychiatric emergencies. Objections have been raised that intravenous narcosis introduces the risk of sudden and irrevocable toxic effects, whereas the truth is that the slow injection of a dilute solution is the safest and most accurate method of estimating the correct dose.

Continuous Intravenous Narcosis An excellent account of the technique was given by Hamilton Bailey, who described the value of giving intravenous saline continuously for a period of 3 to 5 days. He also indicated the value of giving simultaneous intravenous medication—the appropriate drug being added to the saline, which can be infused and regulated with mathematical precision.

Infusion Technique—The technique described is a modification of Bailey's. We assume that the general principles are known. Either a gold-plated cannula or a special needle may be used. The advantage of the special needle is that it is quicker and easier to insert in a resistive patient.

The choice of vein is a question of convenience, and it is found equally satisfactory to use the back of the hand, the front of the forearm, or the lower extremity.

The Solution—The most useful solution is 5% glucose in normal saline, and it is recommended that 10 units of insulin be added to every 500 cc of glucose solution. Several methods are advocated for regulating the temperature of the fluid. This, however, is relatively unimportant, and is far better to keep the patient warm with extra blankets and hot bottles.

Rate of flow—The rate of flow is regulated by a thumb-screw to about 30 drops per minute. The narcotic is injected into the tubing just proximal to the needle, and this is repeated in minimal doses whenever the patient becomes restless. There is no fixed rule for determining the maximum dosage or the maximum duration of infusion. These must be decided entirely by clinical experience, together with the general condition of the patient. In our experience it has been necessary in severe cases to inject as much as 3 grm of soneryl during the first day. This somewhat excessive dosage

seems to be made safe by extreme dilution and very slow administration in saline. The infusion may be continued in most cases with reasonable safety for 48 hours, by which time it is possible to revert to ordinary methods of treatment.

1 The patient must be under constant observation

2 Chart the pulse and respiration every 15 minutes and the temperature and blood-pressure every 4 hours

3 Regulate rate of infusion to between 20 and 30 drops per minute

4 Look for swelling under the eyes or in the limbs

Important—The nurse must report at once

(i) Pallor or cyanosis

(ii) Pulse-rate below 45 or above 90

(iii) Any respiratory distress

Case 1 Married woman aged 24 Puerperal confusional state. There was no personal or family history of epilepsy or psychosis. The present illness was of sudden onset on the fourth day of the puerperium. During the first two days ordinary methods of sedation and tube-feeding completely failed to effect any improvement, in fact she was becoming more ill. Continuous infusion of saline was then begun, together with an initial dose of 1 grm of soneryl sodium. During the following 24 hours the infusion was continued at the rate of 30 drops per minute, together with 2 cc of 10% soneryl approximately every hour.

II *Prolonged Narcosis with Soneryl Suppositories*—Many exponents of somnifaine therapy aim at producing a deep sleep from the very beginning of treatment. This method fails to allow for possible idiosyncrasy, and is not without danger. We prefer the method advocated by Meeloo of using the first three days as a test period to determine the individual reaction of each patient.

The initial narcosis should be controlled by doses which do not exceed 5 gr every 6 hours. It is often sufficient to give 5 gr twice or thrice daily. The most important feature during the test period is the condition of the pulse, a pulse-rate below 50 being the commonest sign of intolerance. After 3 days, subject to the general condition being satisfactory, it is safe to increase the dosage. The maximum single dose is 15 gr, but 10 gr repeated two or three times a day is usually adequate for producing a fairly continuous and deep sleep. In connection with dosage, it is advisable to consider the routine administration of insulin. Glucose, being an essential ingredient of a nutritious fluid diet, is given as a matter of course. The addition of insulin is believed to raise the tolerance to soneryl and to necessitate larger doses. Therefore, insulin is reserved

for cases showing ketosis. Slight acetonuria occurred in about half the present series, but it was never severe, and always disappeared on giving insulin, glucose and copious fluids.

Some patients are managed easily and sleep almost continuously with the smallest doses, others respond to large and frequent doses. The ideal is to produce continuous deep sleep, unaccompanied by toxic effects. This is seldom achieved, and yet, in cases where sleep is by no means continuous, the results are almost as good. A study of such cases shows that although the drug does not necessarily produce sleep, it invariably produces other effects described collectively as "barbital intoxication". In such cases the effects of narcosis may be paradoxical, consisting of acute hallucinatory excitement and motor restlessness throughout the period of intoxication, followed by sudden complete recovery a few days after abstinence.

Duration of Narcosis The optimal duration of narcosis is quite uncertain, although the general consensus of opinion is that a period of not less than 10 days is required. In the absence of definite criteria we prolong most narcoses for an arbitrary period of 14 days. Nevertheless, in cases with toxic complications and consequently abbreviated treatment, the results were equally good.

There is another side to the question of duration. Certain writers have referred to very prolonged periods extending over several weeks, or even months. Their reports of success in seemingly hopeless cases appear to justify this unusual procedure.

Secondary Effects (1) Cravings (2) Catatonia. Thorner observed the same effect and ascribed it to the inhibition of higher inhibitory centres. This mechanism is believed to explain the action of soneryl in those cases where it is effective in interrupting the negativism of catatonia.

(3) *Post-Narcotic Epilepsy* "The patient had four epileptiform convulsions in the next twenty four hours. Her symptoms suggested calcium deficiency and she was treated with calcium by the mouth. Her symptoms subsided completely."

There are indications suggesting that tetany rather than epilepsy is the correct description of post-narcotic convulsions.

The reported incidence of post-narcotic epilepsy is about 1% but it is possible that careful observation of patients after treatment for signs of tetany would show that this is more frequent.

Conclusion It may be compared with somnifaine narcosis, and even if the recovery-rate is rather lower at least the toxic complications are less common.

IV *PROLONGED NARCOSIS WITH PARALDHYDE AND DIAL* Brody (Jour. Ment. Science, May 1940) discusses the

use of paraldehyde and dial in producing therapeutic narcosis. The paraldehyde is prepared as a suspension in the strength of $1\frac{1}{2}$ drms of paraldehyde and 1 minim of liquor atropinae to the ounce. Dial is given $1\frac{1}{2}$ gr tablets which may be crushed into the draught. The normal dose is 1 oz of paraldehyde mixture and one tablet of dial. The draught is further diluted with water for each dose. Even so, it is very unpleasant, and many patients like to suck a slice of lemon with it.

The first dose of the day is given about $\frac{3}{4}$ hour after breakfast, and nearly always needs to be repeated in the evening. Many patients sleep quite satisfactorily on these two daily doses, but others need a further dose during either the afternoon or the night. This extra dose should be of the paraldehyde mixture only, without dial, so that dial is not given more than twice in 24 hours. Sometimes the dosage has to be increased after a few days. If so, double doses of paraldehyde mixture and 2 tablets of dial are given as required. Not more than 3 double doses of paraldehyde mixture (= 9 drms of paraldehyde) and 4 tablets of dial (= 6 gr of dial) should be given in 24 hours, though this dosage may be maintained for several days. In order to keep the technique as simple and uniform as possible, the rule should be—not more than 2 doses of paraldehyde and dial together, plus one extra dose of paraldehyde alone during 24 hours, whether in single or double strength. Experience taught that increasing the dosage beyond this level or doubling the dose of one without the other, or giving smaller doses more often, complicates the technique without improving the result.

The normal hospital diet is given, but avoiding anything that might be difficult to swallow, such as bread crusts or roast meat. Mince, stews, mashed vegetables, eggs, soft bread and butter with jam are all safe. Also, the patient has two to three pints of egg and milk mixture daily, and liberal glucose and lemon drinks. Solid food is taken as long as the patient can feed himself without difficulty in swallowing. If he cannot feed himself or there is the slightest dysphagia, he is given fluids only.

Diet and medicine are given when the patient wakes up, not at fixed times. Very often, having eaten, the patient will fall asleep again. In any case the medicine should not be given until $\frac{3}{4}$ hour after meal, since giving it earlier increases the liability to vomit.

Insulin is not given so long as the patient can take solid food, which he generally can for the full course of treatment. If he is reduced to fluids only, 10 units of insulin, which may be increased if necessary, and a glucose drink are given with each dose of medicine.

Narcotic Effect. Ninety patients were treated. The average time out of 24 hours spent fully asleep or drowsy was 17.2 hours.

Complications Dysphagia and ataxia also were uncommon. *Vomiting* was the most troublesome complication. At first, liquor atropinae was not included in the paraldehyde mixture and 15 out of 21 patients vomited. Out of 69 patients who had paraldehyde with liquor atropinae 21 vomited—a striking proportional improvement.

Ketonuria and Glycosuria Only five patients had *ketonuria*. In three cases the patients were so restless that for several days they had not been able to take solid food, and had had fluids only. In two of these insulin was not given, and *ketonuria* ceased when the narcosis ended, and they began to take solid food again. It is not possible to decide whether the end of narcosis itself or the resumption of solid food caused it to disappear. The third patient first showed *ketonuria* on the 6th day. Thereafter he had 10 units of insulin with glucose with each dose of the mixture, but *ketonuria* appeared on the 9th, 10th, 15th, 16th, and 17th days. He was restless and on fluids only throughout. A fourth patient had *ketonuria* on the 9th, 10th, and 11th days when acute otitis media was discovered and the treatment was stopped.

Six patients had *glycosuria*. One of them had *glycosuria* and *ketonuria* together on the 6th and 15th days. Two patients had a "faint trace" only on two occasions each, and the others no more than "a trace" once each. Except in the first patient there were no special associations with the *glycosuria* and it disappeared without special treatment.

K A J L

SULPHADIAZINE IN BURNS

K L Pickrell of the Department of Surgery, Johns Hopkins Hospital (Johns Hopk Hosp Bull, 1941, 69, 217), in a preliminary note records the results obtained in the treatment of 115 burnt patients with 3% sulphadiazine in 8% triethanolamine. The results have been so good that it has been decided to continue the use of this method in the treatment of all burns at the Johns Hopkins Hospital for the time being. A patient whose burns are severe enough to need treatment in hospital is placed at once on sterile sheets in the accident room and treatment for shock is immediately instituted. Cultures are taken from the burnt areas. While the surgeon is scrubbing up, the nurse sprays the burnt areas with the sulphadiazine mixture. The burnt areas are not washed or cleansed in any other way. Spraying is continued every hour on the first day, every two hours on the second day, every three hours on the third day and every four hours on the fourth day. Pickrell points out that sulphadiazine can be safely used in and around the eyes with impunity. It can be detected in the blood within some hours after having been sprayed on the surface of the burn.

L I I

ROENTGENOSCOPY AS A DIAGNOSTIC AID IN CORONARY OCCLUSION

Master, A M, (Am J Roentgenol 45 350, 1941) records roentgenoscopic observations of ventricular contraction in 300 private patients. More than half of these had coronary occlusion, the remainder included other types of heart disease and normal subjects.

The technique employed is described in detail. Roentgenoscopy is shown to be a simple and inexpensive method of diagnosing coronary occlusion with myocardial infarction.

Abnormalities in pulsation were present in 75 per cent of the cases of coronary occlusion. Systolic expansion (reversal of pulsation) of the left ventricle, observed in 50 per cent of these cases, is characteristic, if not pathognomonic, of myocardial infarction. "Lag" and "doubling" of pulsation are incomplete forms of systolic expansion. Systolic expansion is seen in practically every case of large heart with ventricular aneurysm. Absence and diminution of pulsation were present in 25 per cent of cases with coronary occlusion, but also occurred in other types of heart disease.

The abnormal pulsations observed were located in the apical and the supra-apical portions of the left ventricle in almost 85 per cent of the cases studied.

The incidence of abnormal pulsation in coronary occlusion was found to be greater when the heart was enlarged. When the area of abnormal pulsation was large, the prognosis was poor.

Systolic expansion may appear directly after the coronary occlusion and persist for many years. Its disappearance, or a change to absence or diminution of pulsation, is of favourable significance.

In normal hearts the pulsations are always normal. Hypertension alone does not produce changes. Disease of the coronary artery, without occlusion, did not exhibit systolic expansion or absence of pulsation. When these conditions are present, coronary occlusion should be suspected. Systolic expansion is seen occasionally in cases of aortic insufficiency with cardiac enlargement.

Roentgenoscopy should form part of the routine examination of every cardiac suspect. It may be positive when the physical examination and electrocardiogram are negative.

Author's Summary

GROWTH AND THE DIABETOGENIC ACTION OF ANTERIOR PITUITARY

It has been known by previous works of the author and others that crude extract of the anterior pituitary produces temporary and

permanent Diabetes in animals especially in dogs Before an animal becomes diabetic it puts on fat and nitrogen retention occurs There is hypertrophy of the islets of the Langerhans Joslin has mentioned that about 80% of his adult diabetic patients are or have been, over weight at the time they come for treatment and excessive weight is widely recognised as a frequent characteristic of the elderly diabetic patient F G Young, (*Brit Med J* 1940 II 897) by his experiments on young puppies has tried to show that the same crude extract of the fresh anterior pituitary which produces diabetes in the adult dogs produces growth if it is injected in the dog puppies The author by his experiments and evidences from previous investigations shows that the same pituitary extract may be essentially growth (weight)-promoting or essentially diabetogenic according to the age of the animal and the adequacy of its pancreatic function In the intact adult animal (dog or cat) both responses may be manifested simultaneously, although the diabetogenic effort ultimately becomes predominant, while in the young puppy the only obvious response to the treatment with the extract is that of accelerated growth

Young quotes Coggershall and Root who find that at the onset of diabetes a substantial proportion of the diabetic children are above the average height for their age and many of these show precocious physical development Joslin in discussing these facts asks a pertinent question "In the child growth is vertical and in the adult it is lateral Is not each type of endocrine origin?" Young's article brings out evidence that it may be due to anterior pituitary Pre-diabetic increase of height in children and of weight in adult, can be regarded as a reactive or protective mechanism for the storage of the carbo-hydrate of which the oxidation is suppressed and often nitrogen which is retained under the influence of the anterior pituitary action The expansive capacity of the adult and growth of the child is definitely limited There will come a point at which carbohydrate, the oxidation of which is inhibited can no longer be completely stored in the form of extra body tissue Sugar then leaks into the blood stream and despite a subsequent and complete subsidence of pituitary overactivity, permanent stigmata may remain in the form of islet lesion and a persistently diabetic condition

J C P

CONCENTRATED RED CELL SUSPENSIONS IN ANAEMIA

Due to emergency blood banks have been established everywhere Blood transfusions are done not only in urgent cases of Haemorrhage and Shock but also in the more severe and resistant cases of anaemia Large scale preparation of plasma from stored blood however, has made available considerable quantities of red blood cells in concentrated form The loss of these red cells, amounting to about 50% of the original volume of whole blood in view of their utility in the treatment of anaemia is particularly regrettable Williams

Davie (Br Med Jour II 641 1941) utilised concentrated suspensions of red cells separated from plasma (which was utilised for drying for the treatment of anaemia). This is done by passing a sterile needle through the cap of the blood bottle and sucking off the supernatant plasma. After removal of the plasma the needle is passed down to the bottom of the remaining red cell layer and red cells are then in their turn sucked off into another bottle. A rather sticky layer of white cells debris platelets and fibrin is left behind. Williams and Davie found no difficulty on account of viscosity and so they added no diluting fluid to all their suspensions. The cells of the suspensions are grouped, cross matched a suspension of 500 cc are prepared by collecting red cell suspensions from one or more bottles. These are stored in the refrigerator for 48 hours after which time those not used are discarded. Concentrated suspensions were used only for cases of chronic anaemia which require rapid replacement of haemoglobin and red cells but minimal increase of circulating blood volume. This was not used for emergency or urgent measure as whole blood and plasma was available everywhere. They emphasize the importance however of regulating the flow to not more than 100 ccm an hour in order to avoid the risk of cardiac embarrassment in anaemic patients who might be expected to have damaged myocardium. They used it in four groups of anaemia: (1) Post haemorrhagic anaemias (2) Anaemia associated with severe infections (3) Anaemias of pregnancy and purpura (4) Dyshaemopoetic anaemias. To compare the individual responses the percentage rise in haemoglobin for each case was calculated for a "standard transfusion" of 500 cc (approximately one bottle) of concentrated red cell suspension. Irrespective of the nature of the condition causing anaemia transfusion with one bottle of 500 ccm raises the haemoglobin between 10% and 12%. Exceptions to this rule occur. Reactions following this transfusion with red cell suspensions are less than whole blood, they also describe a group of reactions which they considered allergic in origin, one of which proved fatal. The authors suggest that all donors with a history of allergic manifestations should be excluded.

J.C.P.

SOME EFFECTS OF VITAMINS B AND C ON SENILE PATIENTS

W Stephenson, C Penton, and V Korenchevsky (Brit Med Jour II 839, 1941), treated forty senile patients with Vitamin B complex and C, the whole period of observation lasting for about a year. The condition of these patients were compared with that of 18 senile patients of a control group receiving dummy tablets. All the patients were on a usual hospital diet not rich in vitamins.

Treatment with Vitamin B and C as with any other remedy did not stop the biologically inevitable development of senility and therefore did not affect those basic features which are specific for and

present in even the most physiological type of senility By treating the aged people with vitamins however, it was possible to prevent or improve in some cases to a striking degree certain of those senile features which could be considered pathological because they appear prematurely or in extreme degree (e.g. muscular, cardiovascular and mental deterioration) or which do not seem to be inevitable in normal physiological senility (e.g. dementia, insomnia, skin rashes and itchings, constipation) During the period of observation improvement or disappearance (apparently not of a lasting nature), of some pathological senile features was observed in numerous cases while a number of other cases were not improved by the treatment and a few patients who had been free from certain senile features developed them during and notwithstanding the treatment It is suggested by the authors that in some suitable cases there might be considerable relief of some pathological senile features by the treatment with vitamins B and C

Authors show that in old people there is also considerable amount of partial or latent Vitamin deficiency as many Specialists in modern Science of nutrition have emphasized it to be widely prevalent in the population of various countries Administration of Vitamins to old persons will result in prevention of certain Vitamin deficiency diseases and there will be fewer manifestations of pathological senility

J C P

DIAMIDINO STILBENE IN KALA-AZAR

Adams and Yorke, and Adler and Rachmilewitz, both in 1939 published papers reporting a few cases of Kala-Azar treated successfully with Diamidino Stilbene Napier and Sen in 1940 published a preliminary paper on the treatment of Kala-Azar by the same drug with good results Since then a number of other reports have been published of successful use of the drug in the treatment of Indian and Sudanese Kala-Azar and Trypanosomiasis Napier, Sen Gupta and Sen (Ind Med Gaz 77 321 June 1942) report their experiences in the treatment of the Kala-Azar with this drug in 100 cases

The patients were treated in Carmichael Hospital for Tropical Diseases in Calcutta and belonged to all communities Majority were Indian males In nearly half the cases the disease was more than 6 months duration Diagnosis was made by demonstrating the parasite in all except two cases Both these cases were children

The specific treatment was given after a week's stay in hospital The patients were on hospital diet and no other treatment was given This treatment was given particularly in resistant cases (cases in which adequate treatment with neostibosan or urea-stibline had failed) Daily, intravenous injections of one per cent solution of the drug was given in all cases except five where intramuscular route was used, it is very painful but seems effective Dosage seems to be

in experimental stage but the scheme followed was as follows In an adult 0.025 gm as initial dose followed by 0.050 gm 0.060 gm 0.075 gm 0.090 gm and 0.100 gm provided the reaction after each dose was not a very severe one and provided the dose did not exceed 0.001 (one milligramme) per pound weight of patient In children the dose was larger and they tolerated the drug better In majority of cases 10-12 doses were given, in some it was increased up to 15 doses The mean total dosage in the 75 cases was 0.597 gm and in 'resistant cases' it was 0.884 gm Some of the reaction following the use of the drug are given here A burning sensation all over the body, flushing of the face, nausea, vomiting, epigastric distress giddiness, palpitation, sweating and occasionally collapse In majority of the cases there has been fall of systolic and diastolic blood-pressure which can be prevented by previous injection of adrenalin Majority of the symptoms are histamine like effect There was no hypoglycaemia following the use of the drug There were some nervous symptoms in about 9 cases i.e. subjective disturbance of sensation over various parts of the trigeminal area, paraesthesia, anaesthesia formication and hyperaesthesia (2) Loss of sensation of light touch over this area with preservation of sense of pressure and pain with no other evident neurological disorder The immediate result of the treatment was that 98 patients were cured and two died Subsequently two of the patients relapsed and one was treated a second time with this drug There was clinical and haematological improvement with increase in total leucocytes Authors conclude that introduction of 4,4-diamidino stilbene is a very great advance in the treatment of Kala-Azar It compares favourably with neostibosan The results obtained in the treatment in the antimony resistant cases are almost as favourable as those in ordinary cases Gramme for gramme Diamidino Stilbene appears to be at least 4 times as effective as Neostibosan There is no evidence in authors' limited experience, that the drug is of any value in the treatment of dermal and cutaneous Leishmaniasis

JCP

CORRIGENDUM Please add the following words after the word "out" in the 2nd line from below on page 359 in our August issue, (Heilig and Visweswar) —

anthelmintic treatment, unimpeded by the undiminished hookworm

The Indian Physician

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LIVERGEN

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 Psychotria and Tenebreck
 Hygrophila Spinosa
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The Indian Physician

VOL 1 NO 10

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Let us remember

THE APHORISMS OF CORVISART

(In 1919 Paul Busquet, librarian of the Académie de Médecine of Paris published a book entitled *The Aphorisms of Clinical Medicine by Corvisart*. The manuscript was originally prepared by one of Corvisart's pupils F V Merat, and was found in the archives of Académie de Médecine. Corvisart, disliking the usual practice of teachers who dictated the matter, established an informal oral course.

Like Stoll and Baerheave, he was partial to the style of Aphorisms which includes a great deal in a few words. With Stoll he declared: I like to have the observed facts expressed accurately and simply and the principles which may be developed therefrom presented with forced clarity.

In this manner were developed the aphorisms which he taught to his pupils and which he never had time to prepare for publication. They form a third section of a manuscript by J V Merat, entitled *A Course of Clinical Medicine by Baron Corvisart with Aphorisms concerning Certain Diseases Collected from the Lectures of this Professor*. The sayings of this creative genius of medicine are full of clinical wisdom and may be read with interest even by the modern physician and we reprint some of these from the translation by A M McDonald M D, *Annals of Medical History*, 1939 p 383 471 546, 1940 p 64.)

Generalities

I Medicine is not the art of curing diseases, it is the art of treating them, with the aim of relieving, of soothing or contenting the patient. We well know that the first definition will often be false.

II The great majority of diseases are complicated. If any exist which are simple, they are most rare.

III Diseases never follow the same pattern, even those which are placed in one group. There are no more two diseases identical in course than there are two leaves of a plant exactly similar.

IV In medicine, there are instances where the most profound human wisdom is unable to anticipate the course or predict the outcome. The really honest physician, therefore, will have no hesitancy in acknowledging his ignorance.

V In obscure cases, one must maintain a wise reserve and observe the natural course of the process, instead of rushing ahead and playing the savant, as is so frequently done. The latter conduct can only partake of presumption or ignorance.

VII In accepting innovations, the physician must be exceedingly conservative In the case of new words, these must not be adopted till the necessity for them is well proved If it is a question of nomenclature, since this is quite foreign to the practitioner, it should give him little concern However, when a new remedy is offered it is highly important that this be accepted only after special trials, carefully checked, have demonstrated its value

VIII. The medical practitioner who would be truly useful should devote himself to the treatment of the particular disease, rather than to discovering to which group it belongs

X When a case appears obscure and there is no risk in the choice of treatment, one should restrict himself to general methods until he has better information (*diagnosis incerta, standum in generalibus*—Stoll)

XI A considerable number of diseases are hereditary, even certain ones which we do not usually recognize as such In general, the morbid conditions of the parents often explain many of those found in the individual under consideration One should, therefore, always inquire carefully concerning illness of the father and mother

XVIII Given diseases vary from year to year, but it seems that the duration, and in the course of some years, the very nature of the prevailing diseases, change For example, twenty years ago, illnesses characterized by delirium and violent mania were quite common, while now they are unusual This observation has been made in the same hospital and upon the same number of patients

XX One may always distinguish apoplectic stupor from all other types of morbid somnolence by examining the pulse, which in these cases should be of good volume, bounding and low

XXIII In the case of many diseases, the curative indication is easy to comprehend, but is difficult or impossible to fulfill One is aware, for instance, that in apoplexy it is necessary to relieve the brain from the effusion which has caused the attack, but we do not know how to accomplish this end

XXIV In very obscure cases one is reduced to the method of trial One must take care that the remedy is not worse than

the disease Above all, it should do no harm (Primum non nocere)

XXV Provided a given therapeutic agent is not contra-indicated, one may permit its use, even if there be little hope of successful result

XXVI In all diseases which terminate in cachexia, fluids accumulate in the body cavities The resulting effusions do not constitute diseases in themselves

XXVII The pain produced by an attack of the itch is different from all others, it is piercing and burning, according to description of patients

XXVIII Ordinarily, we are accustomed to discontinue any very active therapeutic measures during a woman's menstrual period This is a custom from which the practitioner learns to swerve It is a matter of experience that one may without the slightest harm, purge, puke, bathe, or bleed women patients during menstruation This is especially true in emergencies Whenever there may be any question of periculum in mora it is wise to disregard this statement Because in cases where a short delay is of no consequence, it is better to give way to prejudice and withhold the measures to be employed for a few days

XXIX The physician must carefully restrain himself from the mania of attempting to explain everything He must remember that nature, concealed as she is in many of her phenomena, is especially so in morbid anatomy He can only be an observer of Nature, never her confident

Symptomatic Medicine

XXX We mean by "symptomatic medicine," that which treats only the apparent symptoms of a disease However, we thoroughly understand that to cause the complete disappearance of the symptoms, one must secure the elimination of the pathological process itself

XXXI We practice symptomatic medicine (expectant treatment) in all instances where the causal agent of a disease is unknown, or being known, is indestructible

XXXIV. From this we must conclude that in three-fourths of the cases, we knowingly practice symptomatic medicine and

in the other one-fourth this is often done unconsciously. There are a number of instances where one uses only symptomatic measures though he believes he is attacking the basic cause. We are often deceived in this matter.

XXXV One must proceed from day to day, that is to say according to the symptoms and phenomena which present themselves, in the practice of symptomatic medicine. However, in constitutional disorders, the cachexias, etc., the symptoms vary at almost every moment, so if one wished to treat each of them, there would be days when it might be necessary to change treatment ten or more times.

XXXVI Generally speaking, in these diseases as in all others, one must overlook the minor symptoms which are often ephemeral and of short duration, and may or may not depend upon the principal cause. Having cured the latter, the symptoms disappear, either spontaneously, or as the result of treatment.

Delirium

XLIII In all diseases, the presence of delirium is an unfavourable complication. When it represents the principal characteristic of the illness, it is unfavourable in proportion to the intensity and duration of the delirium.

XLIV There are remarkable differences in the manner in which a patient suffering with an acute disease becomes delirious. Either there is a constant confusion and wandering of ideas and he talks incessantly, or he obstinately follows a single train of thought and pursues it to the most minute detail.

XLV There is a tranquil delirium which occurs during certain of the continued fevers, especially towards the final stage, which is due to deficiency of the circulation.

Percussion of the Chest

XLVI Percussion of the thorax is the best touch-stone which we have to investigate or at least to clarify our knowledge concerning many of the lesions of this cavity. By its means we may demonstrate an increase in the volume of the heart, congestion of the lungs, effusions into the pleural cavities, the location of an abscess cavity (vomica), or a tumor, etc. One may even go so far as to estimate the severity of a lesion.

XLVII One must become accustomed to recognize the normal percussion note, heard over a thin chest wall in order to judge the difference in diseased conditions and to be able to determine the severity of the lesion Likewise, one must be familiar with the regions of the chest which are normally less resonant These are the scapular region, that of the vertebral column, the lower portion of the right thorax because of the presence of the liver, and the mammary regions when the breasts are excessive in volume The sternal region is normally more resonant than other areas of the thorax

XLIX One may satisfy himself of the exact extent of the pulmonary lesions by distinguishing the areas which are resonant from those which are not This one can determine in going over the entire thorax In a region where resonance is entirely lacking, one speaks of the resonance of the thigh (*tanquam percussu femoris*—Stoll), which is exactly the effect

L When one percusses a healthy chest one is conscious, after a little practice of the elasticity and resilience of the lungs under the fingers, a sensation which is absent when the organs are consolidated and non-crepitant By means of this tactile sense a deaf person may make use of percussion

The Invasion of Diseases

LII A given disease almost always has two periods of invasion the first, during which patients present some mild symptoms, but nevertheless continue their occupation, the second or actual onset, when they are forced to go to bed This distinction is more striking in the antheumatous lesions This fact concerning forms of invasion has permitted the physician to choose sometimes one, sometimes the other date of onset, according as he has occasion in calculating the critical days and explaining the phenomena which develop

LIII Every illness, even those which seem similar, is subject to variation as to onset and invasion The accounts of patients show us, that in respect to duration, intensity, continuity, or intermittence, various symptoms such as chills, fever, etc, occur differently It is therefore wrong to say that a given disease always develops in this or that particular manner

Crises

LIV The septenary days of the ancients and in general all critical days, have no peculiar significance in the course of any disease. Numerically speaking, there are no truly critical days.

LV Only rarely are there abrupt crises in the diseases which are susceptible to them

LVI Should one apply the term "crises" to sweats, to evacuation of the bowels, to hemorrhages, to voiding of the urine, to expectoration, etc which do not influence the course of the disease?

LVII Most diseases tend to improve or grow worse, little by little (*partitum*) and only gradually come to increase or decrease in severity

LVIII However, the art of medicine should sometimes serve to produce a crisis artificially, or to assist in bringing about those which are impending, or are incomplete

LIX It is difficult to explain how a few crusts (*herpes*) which appear about the lips during the course of certain diseases are sometimes considered to be of favourable portent

Concerning Peripneumonia

LXIII Percussion, together with other signs of this disease, is the most valuable means we have of making a diagnosis. It is necessary to practice percussion repeatedly, in order to know whether to consider the process as increasing or declining

LXIV In peripneumonia, when the posterior portions of the lungs lose their resonance, this is a more unfavourable sign than when the anterior portions are thus involved, because it is evidence that the most voluminous parts of the lungs are affected by the disease

LXV If, during an attack of peripneumonia, resonance is absent over an extensive area of one side, *a fortiori* if this involves the entire side, we may predict the approaching death of the patients whatever the other symptoms of the disease that may be present

LXVI During an acute fever, flushing of the cheek does not always indicate which side of the lung is involved in the

disease It has even been noted that, sometimes, the redness appears on the opposite cheek

LXXI We may, when it is necessary and the measures are indicated, apply all three of these methods in turn At the onset one may do an appropriate bleeding, then use an emetic, and afterwards apply a blister

LXXIV The prognosis in all peripneumonias is always grave and often is most unfavourable

LXXV. In many peripneumonias, and notably in those which are associated with weakness or asthenia, the patients die from an actual suffocative catarrh

Cough

LXXVIII In a simple catarrh, the effort of coughing will sometimes loosen particles of blood, which may be imputed to an inflammatory lesion of the chest However, the absence of fever and the lack of difficulty in respiration, together with the clear resonance on percussion over the chest, should prevent error in this respect

LXXIX Certain aneurysmal tumors or those of other nature may, through pressure on the lungs, trachea, or bronchi, set up a mechanical cough

Metallic (Lead) Colic

LXXX Metal colic is a disease which attacks workers who use certain metals especially lead or its salts, those who live in an atmosphere contaminated by this metal even without actually touching it, and finally, those who take into their bodies substances which contain lead as an ingredient

LXXXI The chief characteristic symptoms are more or less sharp intestinal pains, retraction of the abdomen with little or no tenderness on pressure, constipation and the absence of fever We must have the combination of all of these symptoms because no one of them is pathognomonic

LXXXII In the absence of treatment, or as the result of inappropriate treatment, or of that improperly administered, lead colic tends to degenerate into a paralysis of the upper extremities

LXXXV The only suitable treatment is that spoken of as "La Charite," which consists of purgatives, sudorifics, and narcotics. Cure usually takes place in less than fifteen days.

Putrid Fevers

XCI Tympanites is a most distressing symptom of putrid fever. It has been noted in this connection, that there are two types of tympanites, one of which has its source in the intestine, the other which has its origin in the peritoneum. The form of tympanites in the putrid fever belongs to the first type. It is evidence of atony of the intestine and is caused by the part being distended with gas, a distention which is possibly still more favoured by tonic medicines commonly used in treatment of these fevers.

XCIII In certain of the putrid fevers accompanied by excessive bodily heat, where the lips, gums, teeth, and tongue are encrusted with thickened material, contaminated air reaches the lungs and there causes the inflammations which are found at autopsy in the bodies of individuals dying of this disease.

The Intermittent Fevers

CI Most of the characteristics which are said to distinguish the intermittent fevers from each other, are obscure and unreliable. The only means of orienting oneself among those which recur every day, is to observe the nature of the paroxysms. If these are of equal intensity, the fever is "quotidian," if a more severe paroxysm occurs on alternate days, the fever is a "double tertian," if there are two days with mild attacks followed by a more severe one, it is a "triple quartan," etc. As for the attacks separated by an interval of more than one day, there is no mistaking these.

CII It is wrong to assume that all attacks of intermittent fever proceed in their course according to the manner described by most authors: chill, fever, sweat. One occasionally sees this order lacking and at other times the sequence is reversed, that is to say, there is first the sweat, then the flushing, then the chill. Sometimes there are intermissions between the first two periods of the fever, and the third. We quite frequently note that the chill and flushing occur during the day and sweat does not take place until night.

CIII When the sweat does not definitely terminate an attack of intermittent fever, the fever is usually more obstinate, though not necessarily more dangerous. However, a dropsy sometimes develops, then the disease becomes aggravated.

CV—CVI When the paroxysms of an intermittent fever are stationary, constant, and similar in all particulars, when at the same time there are no signs of gastric or other lesions, this is an indication that these fevers are due to a nervous temperament. One may in such cases, neglect them.

CVII We may give kino boldly in the intermittent fevers when we are sure there is no congestion, no dropsy, etc. which is easily ascertained by the satisfactory condition of the patient on the intervening days, and by experienced examinations.

CVIII The veritable febrifuge which alone is needed when it is necessary to terminate an intermittent fever, is kino. After the fever has been terminated by the use of this drug, one should continue its use for some time in order to prevent a recurrence.

CIX When the decoction of kino has no effect upon an intermittent fever, the solid extract will be more sure in its action.

CXI It is by no means necessary to purge a patient who has just recovered from an intermittent fever. Purgatives given at this time have often caused a recurrence of the fever.

Heart Disease—Causes

CXXVIII It is quite possible that heredity may be a frequent cause of diseases of the heart. We know that gout, asthma, apoplexy, phthisis, calculus of the bladder, often depend on this factor alone.

CXXX From the time of birth, there may be present disproportion between the different parts of the heart, and the vessels which leave it, due to faulty structure, conditions which could not fail to lead to organic lesions.

CXXXIII Persons of florid complexion, plethoric individuals, those who lead a sedentary over-nourished existence, are predisposed to disease of the heart because of the continued overfilling of the vascular system.

CXXXV Habitual dyspnoea predisposes to enlargement of this organ (heart) by the resistance which is thereby offered to the circulation

Symptoms

CXL The Symptoms of diseases of the heart are quite numerous These include the face is more or less highly colored (florid) somewhat puffy and swollen; the lips, sometimes the ears, the alae of the nose are injected and of a somewhat livid color

CXLI Respiration is more or less impeded and difficult, short, noisy, and distressing, especially after the patient has made marked exertion, particularly when he climbs stairs Then the respiratory difficulty approaches almost to suffocation and these patients are compelled to stop in order to regain their breath

CXLII In the precordial region, one feels more or less forcible pulsations which are violent, extensive, irregular, etc In this region, percussion gives a more or less impaired resonance when the disease is somewhat advanced However, during the early stages, resonance is normal The cardiac pulsations may extend into the epigastric region where one feels them quite prominently Very often these pulsations have been mistaken for evidence of aneurysm of the coeliac axis, a condition which is extremely rare

CXLIII The pulse shares the characteristics of the heart beat in most instances It presents, as does the heart, pulsations of varying amplitude, and with more or less irregularity At other times these are faint, of low volume and filiform The radial pulse may vary on the two sides of the body This depends upon the position of the patient or of the arms, or again, upon a special lesion such as a tumor which presses upon the subclavian of one side

CXLIV Beside these qualities, the pulse has in its nature another characteristic of which one is conscious without being able to describe it and which one appreciates only by practice This quality of the pulse has no relation to that presented by other diseases

(To be Continued)

Original Contributions

BENIGN LYMPHOCYTIC MENINGITIS

A REPORT OF 12 CASES IN BOMBAY

By

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My object in presenting these Case Reports of twelve cases of Benign Lymphocytic meningitis is two-fold (1) to stress the importance and frequency of this benign form of meningitis in India, and (2) to familiarize the clinician with a picture of this condition in order to facilitate its recognition. In a monograph on "Benign Lymphocytic Meningitis", published in 1939, I have already presented a comprehensive survey of the world-literature on the subject of benign meningitis, in this same monograph, notes were appended of two cases of benign lymphocytic meningitis observed personally in this country within a short time. My interest in this subject was revived a few months ago, when I happened to come across further cases of this type, in hospital practice.

The earliest case of benign lymphocytic meningitis was reported, according to Gunther, in 1906. The first clear description of the syndrome was given in 1925 by Wallgren, who stressed the following characteristic features, viz (1) an acute onset with symptoms and signs of meningitis, (2) a short duration and benign course, (3) the cerebro-spinal fluid showing a complete absence of organisms, a preponderance of mononuclear cells, a fairly normal chloride content and a raised pressure, (4) absence of para-meningitic conditions like, mastoiditis, encephalitis and herpes.

Benign lymphocytic meningitis has been designated, from time to time, as acute aseptic meningitis, aseptic lymphocytic meningitis, benign aseptic purulent meningitis, acute idiopathic benign serous meningitis, epidemic meningitis serosa, simple meningitis, benign lymphocytic choriomeningitis and as benign

lymphocytic meningitis When first described, benign lymphocytic meningitis was regarded as a "clinical curiosity", while its very existence was doubted by many authors Since that time, so many papers and case-reports have appeared on the subject, from all over the world, that we are left in no doubt whatsoever about the existence or incidence of this entity

A considerable amount of work, both experimental and statistical, has been done in order to elucidate the cause of benign lymphocytic meningitis There was a tendency on the part of earlier workers to identify the disease with encephalitis lethargica or acute anterior poliomyelitis but of late, medical opinion has come to regard it as being of virus aetiology In 1934 while working at the National Institute of Health on the transmission in monkeys of infected material from a fatal case of encephalitis, Armstrong and Lillie, discovered a new virus, artificial inoculation of rhesus monkeys with this virus was shown to produce a clinical entity closely similar to the benign lymphocytic meningitis of man The virus nature of the causative agent of benign lymphocytic meningitis was convincingly proved by the systematic experiments of Rivers and Scott²³, the causative agent of benign lymphocytic meningitis was shown to be (1) invisible and (2) filter-passing, capable of passing through Berkefeld candles The virus of benign lymphocytic meningitis is pathogenic to monkeys (*Macacus rhesus* and *macacus irus*), rats, mice and guinea-pigs Animals resistant to the virus are the dog, ferret, rabbit, hen, canary, parakeet, field-vole and bank-vole Recent work suggests rodents as being the probable reservoirs of infection for human beings, the infection is said to prevail in some strains of healthy mice in Europe and America and transmitted by them to monkeys, guinea-pigs, rats and humans The portal of entry or mode of infection has not been worked out properly, the virus has variously been said to gain an entry into the human body through the skin and mucosae, through the nasopharynx, via the gastro-intestinal tract or by venereal transmission Because of the high incidence of negative serological reports in otherwise typical cases of benign lymphocytic meningitis, we are forced to believe in the co-existence of "non-viral" forms of benign lymphocytic meningitis

Clinical Features In order to facilitate the problem of differential diagnosis, attention is drawn to the following charac-

teristic clinical features observed in cases of benign lymphocytic meningitis (1) *age* no age is exempt from this disease, almost 50 per cent of the reported cases have been under the age of 10, it is seldom met with in individuals over 50 (2) *Sex* a perusal of the literature on benign lymphocytic meningitis reveals a striking preponderance of males (3) *Onset* In the great majority of reported cases, the onset of the disease has been sudden or acute (4) *Symptoms* Headache is usually the presenting symptom, occipital and severe as a rule, it may be frontal or slight Vomiting has been reported in over 50 per cent of cases Other symptoms observed are backache, pains in the legs, aching of muscles, abdominal pain, intractable insomnia, convulsions, delirium, giddiness, diplopia, urinary symptoms, constipation, retching, "continuous yawning" and diarrhoea (5) The *temperature* is usually high, remittent or continuous and comes down by lysis or crisis, there is a tendency to bradycardia (6) *Neurological signs, Meningeal signs*, e g , Kernig's sign, Brudzinski's signs and cervical rigidity, are usually positive The *tendon reflexes* are variable, they may be unduly brisk and exaggerated or absent The "plantars" may be flexor or extensor *Ocular manifestations* e g strabismus, ptosis, photophobia, papilloedema and retinal haemorrhages, have been described *Paralytic symptoms* e g , unilateral and bilateral facial palsies, weakness or loss of power in one or more limbs and deviation of the uvula to one side, have all been observed, other symptoms on record are clonic movements or twitchings of the limbs, face and lips and sensory manifestations like "pins and needles", hyperalgesia and analgesia (7) The total white blood cell count is usually raised to 10,000 or more per c mm , in Toomey's cases, on the other hand, the total counts were usually low (from 3,200 to 5,000) (8) *Course* the duration of the disease is said to vary from 2 days to 4 weeks (9) *Cerebrospinal fluid change*. (A) The pressure is raised (B) The fluid may be clear, cloudy, opalescent or xanthochronic (C) Fibrin webs are definitely unusual (D) The cell-count is variable and may vary from 50 to 2,000 cells Viets and Warren have reported a cell count of 3,975 (E) In the great majority of cases, there is a preponderance of lymphocytes though in a few cases, polymorphonuclear cells are preponderant in the initial phases of the illness (F) The protein and globulin contents are usually raised (G) The sugar content is said to be within normal limits 40 to 70 mg per 100 c c (H) Chloride content may be normal

or slightly diminished, it never attains the low figures of tuberculous meningitis. (I) Organisms are never found, either on direct examination, culture, or guinea-pig inoculation (10) *Prognosis* there is practically invariably, progress towards a complete and lasting recovery, a fatal issue is very rare (11) *Treatment* This is hardly necessary, except along symptomatic lines and to relieve the raised intracranial pressure; specific sera are of doubtful value

Selection of Cases

A study of the Reports of all cases of meningitis admitted to the KEM Hospital, Bombay, within the five year period from 1937 to 1941 (inclusive), was undertaken with a view to determine the percentage incidence of the different forms of meningitis in India. In Table I, are incorporated the results of this analysis.

TABLE I
Analysis of Meningitis Cases (1937 to 1941), KEM Hospital, Bombay

Type of Meningitis		No of cases	% Incidence
1	Meningococcal meningitis	13	0.8
2	Pneumococcal	30	
3	Tuberculous	15	
4	Syphilitic	5	
5	Post vaccinal	2	
6	Benign Lymphocytic	12	
7	Unclassified forms	39	
Total Number of cases		176	

There were 12 cases of benign lymphocytic meningitis in a total of 176 cases of meningitis, giving an incidence rate of 6.8 per cent, all questionable and borderline cases were rigidly excluded. In my previous analysis of Meningitis cases in London, there were 7 cases of benign lymphocytic meningitis in a total of 294 cases of meningitis, the incidence rate being only 2.4 per cent. This is surprising in view of the fact that benign lymphocytic meningitis as a clinical entity is practically unknown to the practising physicians of India while in England, in spite of a lower incidence, it has excited considerable interest and research. The twelve cases of benign lymphocytic meningitis which form the subject-matter of this clinical report, had been variously diagnosed in Hospital as "Tuberculous meningitis," "meningococcal meningitis," "Encephalitis," "Polioencephalitis," "acute meningitis," "lymphocytic sterile meningitis," "specific meningitis" and "meningitis of unknown origin."

Case Reports

Case 1 A Hindoo female, aged 17, was admitted to the K E M Hospital Bombay, on 30th April 1938 with one day's history of headache fever and pains in the back and limbs. The onset of the disease was quite sudden she vomited soon after the onset. On Examination there was severe neck rigidity Kernig's was positive and the pupils were regular equal and reacted to light and accommodation the rest of the nervous system was normal. The throat was congested, tonsils enlarged, tongue coated liver and spleen not palpable rhonchi over both lungs Temp 101°F pulse rate 112 p.m. and resp rate 28 p.m. For C.S.F. findings see Table II. The W.B.C. count was 8200 there being 65% polymorphs 30% lymphocytes 3% mononuclears and 2% eosinophils. Lumbar puncture was repeatedly performed to relieve tension. The temperature which was intermittent to start with became remittent and finally touched normal about the 8th day. She received besides a diaphoretic mixture two 5 c.c. injections of Prontosil intramuscularly. Her general condition improved rapidly and she was discharged cured on the 13th May, 1938 after hospital stay of two weeks.

TABLE II
Cerebro-spinal fluid observations in Case 1

Date	Appearance	Pressure	Cells per cmm	Types of cells	Protein	Globulin	Sugar	Bacteria	Chloride
5.5.38	Slightly turbid	+	75	Lymphocytes & a few polys	0.3%	+	decreased	nil	720
13.5.38	turbid	-	352	Lymphocytes	0.4%	+	markedly diminished	nil	
19.5.38	Slightly turbid	-	71	Lymphocytes	0.3%	+	diminished	nil	

Case 2 A Hindoo male child, aged 7, was admitted to hospital on 11th October 1938 in a semicomatose condition with a history of continuous fever for four days. The onset was sudden and the presenting symptom was headache. On Examination the patient was semi-comatose, there was considerable neck rigidity Kernig's sign was positive the reflexes (knee and ankle jerks) were unduly brisk and the plantar extensors the pupils were dilated but reacted to light there was considerable extension of the neck, while the thighs and legs were kept in a position of flexion. The other systems were normal. Fever was continuous to begin with (from 100° to 103°F) became irregularly intermittent after 3 days (from 98° to 103°) and finally touched normal on the 14th day. During convalescence, there were two further small rises of temperature. The pulse rate (with a temp. of 103°) was 110 and the resp. rate 26 p.m. C.S.F. report (dated 27.10.38) turbid fluid 603 cells preponderance of lymphocytes protein 0.4% globulin increased sugar diminished no bacteria cultures negative. The patient received three or four Prontosil injections. There was a steady improvement in the condition of the patient. The neurological signs disappeared and the patient was discharged cured on the 16th November 1938.

Case 3 A Hindoo male aged 25 was admitted on 10th January, 1939 with a four days' history of severe headache vomiting fever and dry cough. The onset was sudden there was a history of trauma to the head. On Examination he was well built and well nourished the nails and conjunctivae were pale. He was very listless and had a staring expression. The neck was rigid Kernig's negative reflexes normal plantar doubtful pupils equal and reacting well to light. The tongue was coated centrally and rhonchi were heard over the back, constipation was severe Temp 102°F pulse 138 resp 28. W.B.C. count was 7250 with 88% polymorphs 13% lymphocytes and 1% mononuclears. C.S.F. report (dated 11.1.39) fluid clear 9 cells lymphocytes and polymorphs, protein 0.06% globulin increased sugar normal no organisms. The temp. was down to normal within 30 hours there was a second rise of temperature to 103° for 2 days after an interval of 5 days. There was an all round improvement in the patient's condition he was discharged fit on the 23rd January 1939 after a stay in hospital of 12 days.

Case 4 A Muslim boy aged 10 was admitted on 24th May 1939 with a few days history of fever and spasmodic contractions of the muscles of the right side of the body. In 1932 he had suffered from a peculiar fever during which he had lost power in his lower extremities and the power of speech.

On Examination he was thin and wasted there was little or no neck rigidity Kernig's was negative the deep reflexes were lost and the plantar flexor. Peculiar contractions of the muscles were observed on the right side. The other systems were normal.

C.S.F. Report (dated 24.5.39) fluid clear not under pressure 33 cells all lymphocytes protein minimal (0.02%) globulin normal sugar normal W.R. negative no organisms on smear or culture.

The patient recovered completely and was discharged within 48 hours.

Case 5 A Muslim male aged 30 was admitted on 29th March 1940 in an unconscious condition with muttering delirium. There were no relatives or friends to give a history.

On Examination he was well built and well nourished the nails and lips were cyanosed there was a conjugate deviation of the eyeballs to the right the pupils were of normal size and reacted to light the deep reflexes were normal and the plantar flexor. Crepitations were audible all over the chest. Temperature 100°F Pulse 150 Resp 40.

C.S.F. Report (dated 29.3.40) fluid clear under tension 133 cells all lymphocytes protein 0.3%, globulin increased sugar slightly increased chloride 709 mg smears and cultures negative.

The patient's condition deteriorated within a few hours and he died on the day of a mission. The diagnosis was confirmed at autopsy.

Seasonal Incidence 50 per cent of the cases were reported in the months of March, April and May and 33.3 per cent in the two months of October and November

Familial Incidence Not observed in any of the cases

Predisposing Factors In case 3, there was a definite history of trauma to the head prior to the onset of the disease. Case 12 became intensely drowsy and developed signs and symptoms of meningitis about 7 days after a snake-bite

Onset of disease In the great majority of cases, the onset of the illness was acute or sudden, in cases 8 and 10, the suddenness of onset was almost dramatic. In two or three of the cases, the onset was rather insidious and there was a suggestion of a "prodromal phase" with fever, headache and malaise

Symptoms—*Headache* was a prominent symptom in the majority of cases. In two or three of the cases, the onset of the disease was so sudden that a history of headache could not be elicited. In one case, the headache was frontal, as in the majority of Toomey's case, in two or three cases, it was generalized, as in Spero's case. The severity of the headache was variable, in cases 3 and 8 it was intense and agonizing while in two or three cases it was only slight and did not incapacitate the patient in any way

Vomiting was noted in 25 per cent of the cases (cases 1, 3 and 12), in no case, was it of a projectile nature, in case 12, it was associated with intense nausea

Backache and limb-pains were particularly conspicuous in case 1. Giddiness was a prominent feature of case 10, it was the presenting symptom in Dominick's⁶ case of benign lymphocytic meningitis

Convulsions were noted in case 9. In case 4, there were spasmodic contractions of the muscles of the body, epileptiform fits have been described in cases of benign lymphocytic meningitis by Barker & Ford, and by Viets & Watts. *Constipation* was noted in practically all of my cases, this has been so in the great majority of cases on record. *Urinary symptoms* were strikingly absent in the present series, other authors have reported retention of urine, frequency and dysuria in cases of benign lymphocytic meningitis. Restlessness or listlessness was a feature of case 3 while in cases 11 and 12, there was characteristic "drowsi-

ness with insomnia", as described previously by Hughes in cases of benign lymphocytic meningitis. In as many as 50 per cent of the cases, the patients became comatose or unconscious during the course of their illness, in cases 2 and 7, the patients were stuporose or semi-comatose.

Temperature and pulse The temperature was high and of a continuous type in the majority of cases. In case 1, the temperature was intermittent to begin with later becoming remittent, a similar onset with intermittent temperature has been observed by Findlay, Alcock and Stern. In case 2 the temperature, though of a continuous type to begin with, became irregularly intermittent later on. Rigors were prominent in case 7. In as many as 8 out of 12 cases, the fall of temperature was by lysis. In cases 2 and 3, recurrences of fever, lasting for a couple of days, were observed a few days after the initial fall of temperature.

Though bradycardia has been reported in cases of benign lymphocytic meningitis by numerous writers on the subject, it was conspicuous by its absence in my series of cases. In only one case out of 12 (case 7) was the pulse-rate definitely low in relation to the temperature (pulse rate of 88 with a temp of 102°F). As a matter of fact, there was a tendency to a relative tachycardia in at least three of my cases, in case 3, a rate of 138 with a temperature of 102°F, in case 5 a rate of 150 with a temperature of 100°F, in case 9, a rate of 144 with a temperature of 100°F.

Meningeal signs Signs of meningeal irritation, e.g. neck rigidity, Kernig's sign and Brudzinski's signs, were observed in the majority of my cases. In cases 3, 4 and 6, however, the only sign of meningeal irritation was "an increase in the tone of the cervical muscles". In cases 2 and 9, the neck-rigidity was severe enough to cause actual deformity of the head and neck while at rest. In case 7, Kernig's sign was strongly positive and yet there was no cervical rigidity.

Ocular manifestations These were noted in some of the cases. Conjugate deviation of the eyes to the right was observed in case 5, in case 7, the conjunctivae were markedly congested, case 3 displayed a "peculiar staring appearance" of the eyes. In the majority of my cases no pupillary abnormalities were reported. In case 2, the pupils were reported as "dilated but reacting

well", in case 9 as "dilated and fixed", in case 11 as "small but reacting well" and in cases 6 and 10 as "normal in size and reacting sluggishly to light"

Speech Speech was affected in case 7 only, it was described as "peculiar and difficult to understand"

Reflexes In case 4, the deep reflexes were reported as "lost" in all the four extremities, in cases, 2, 10 and 11, they were unduly brisk or exaggerated, in case 6, they were exaggerated on the left side of the body only

The plantars were reported as "normal" or "flexor" in more than half of my cases. In cases 2, 10 and 11, they were definitely "extensor" (Babinski response), while in cases 3 and 6, they were "doubtful". This is interesting in view of Lesne's and Boquien's assertion that extensor plantars do not occur in benign lymphocytic meningitis. Their assertion has been denied by numerous authors in the past.

Paralytic phenomena were strikingly absent in this series of cases, the absence of paralytic manifestations in cases of benign lymphocytic meningitis has been stressed by Armstrong and Dickens.

Respiratory signs There was severe congestion of the throat with enlargement of tonsils in case 1; infections of the upper respiratory tract were observed by Dummer and others in as many as 64 per cent of their cases. Allen and Spencer have also reported congestion of the throat with cervical adenitis in benign lymphocytic meningitis. In cases 1 and 3, rhonchi were heard all over the chest while in case 5, there were rhonchi and crepitations, in the latter case, the respiratory rate was 40 per minute and the nails and lips of the patient showed cyanosis.

Liver and Spleen Enlargement of the liver (three-finger-breaths) was detected in only one of our cases (case 8), splenomegaly was not reported even once.

Blood count In case 10, the total white cell count was unduly high, viz 27,000 per cmm with 91 per cent polymorphs. In a case reported by Findlay, Alcock and Stern, it was as high as 37,200 with 76.5 per cent polymorphs.

In the rest of my cases, the total count varied from 7,250 to 8,200 per cmm. In 50 per cent of the cases, there was a relative

increase of polymorphs and in 16.6 per cent a relative increase of lymphocytes

The blood Wassermann and Kahn Tests were invariably negative with but one exception, in case 8, they were positive

Urine Examination Albumin was noted in the majority of cases. In case 10, acetone was noted in the absence of sugar (Spero's case). Pus cells in fair numbers were observed in 25 per cent of cases. In cases 8 and 10, the urine contained fair numbers of red cells, as in a case previously reported by Allen and Spences

Cerebro-spinal Fluid Reports on pressure of the C S F were very variable. The fluid was reported as "clear" or "transparent" in 8 of our cases, as "turbid" or "hazy" in 3 and as yellowish or "xanthochromic" in one case (case 12)

Xanthochromia has been reported in benign lymphocytic meningitis by Verillote and Le Blaye, by Findlay, Alcock and Stern⁸, by Scott and Rivers¹¹ and by Vakil

The pleocytosis was extremely variable, the cell count varied from 9 to 603 cells per c mm in the twelve cases, with an average count of 206 per c mm. With the exception of case 3, the cell count was invariably more than 30 per c mm. In 5 of my cases, the cells in the C S F were strictly lymphocytes, there being no polymorphs, in four there were mostly lymphocytes with few polymorphs, and in three cases, the cell picture was polymorphonuclear to begin with, later becoming lymphocytic. Case 5, the only case of my series to end fatally, had a cell count of only 133 cells

The protein content of the C S F was above normal in all cases but one (viz case 4 with 0.02 per cent protein). The maximum figure attained was 0.5 per cent in case 9 while the average for all cases worked out at 0.26 per cent. The globulin content of the C S F was normal in one case, slightly raised in three, moderately raised in 6 and markedly raised in 2 of the cases. The sugar content is said to be normal in benign lymphocytic meningitis (40 to 70 mg per 100 c c). In the present series of cases, it was reported as normal in 7 cases, as slightly increased in one case (case 6), as moderately diminished in 2 cases (cases 1 and 2) and as "absent" in 2 cases (cases 11 and 12). The chloride of the C S F in the twelve cases varied from 594 mg per

100 c c in case 11 to 743 mg per 100 c c in case 6, the average value for the series worked out at 693 mg per 100 c c. The chloride content in benign lymphocytic meningitis shows only a slight diminution in contrast to the extremely low figures attained in cases of tuberculous meningitis.

Pathogenic organisms were not found in any of the cases, either on direct examination or in culture.

Duration of Illness The duration of pyrexia varied from a minimum of 2 days in case 8 to a maximum of 33 days in case 11, the average for the series was 12 days. Duration of symptoms before admission varied from a few hours to as long as one month.

Course In as many as 11 out of 12 cases there was recovery, complete and uneventful, there were no complications and no sequelae. In one case only (case 5) was there a fatal issue, the patient's condition deteriorated rapidly within a few hours of admission and death occurred soon after.

Treatment Treatment was along symptomatic lines in the great majority of cases, besides lumbar punctures for relieving intracranial tension, diaphoretics for reducing the temperature, acid Hexamine preparations as meningeal antiseptics, the patients were left very much to themselves. Prontosil was used in cases 1 and 2 and M & B 693 in case 12. In an essentially benign disease like benign lymphocytic meningitis, treatment is hardly necessary, recovery is the rule.

Difficulties in the Diagnosis of Benign Lymphocytic Meningitis

In spite of a fairly recent and massive literature on the subject of benign lymphocytic meningitis, mistakes in diagnosis are very frequent indeed. The most common sources of error, to my mind are (1) *Tuberculous meningitis*. Differential diagnosis between these two diseases has already been discussed in detail elsewhere. The so-called cases of "Tuberculous meningitis with recovery" reported in the literature are, but for a few exceptions, merely cases of benign lymphocytic meningitis. While going through the K E M Hospital reports, I have come across only one case which can truly be labelled as "Tuberculous meningitis with recovery" —

Case Report "A" A Hindu male, aged 30, coolie, was admitted to the K E M Hospital on 2nd August, 1939 with a history of severe headache, pains in the back of the neck and continuous fever for two weeks.

On examination, the man was well-built and well-nourished and preferred to lie on one side (lateral decubitus) with the body curled up, there was twitching of the facial muscles. The pupils were normal, equal and reacted well to light, the deep reflexes were exaggerated, the superficial reflexes were normal and the plantars, extensor on the left and normal on the right side. Neck-rigidity was severe and Kernig's and Brudzinski's signs, positive. The tongue was furred, the abdomen retracted, the liver and spleen were not palpable. Nothing abnormal was detected in the urine. W B C count was 13,750 with 60% polymorphs, 35% lymphocytes, 3% mononuclears and 2% eosinophils. Temperature 101°F, Pulse 100, Resp 26. The fundi showed macular choroiditis.

TABLE VII
Cerebro spinal Fluid Observations in Case A

Date	Appearance	Cells per cmm	Type of cells	Protein	Globulin	Sugar	Chloride	Bacteria	Cob web
28.8.39	Clear	450	Polymorphs	0.5%	++	diminished	567mg	nil	+
28.8.39	Yellow	266	+ Lymphocytes + Polymorphs	0.5%	+	absent	701	nil	+
11.9.39	Clear	~3	+ Lymphocytes + All lymphocytes	?	+	normal	701	Tubercle bacilli found	nil

The temperature, remittent in character, touched normal 5 days after admission. There was a steady improvement in the general condition, the neurological signs disappeared and the patient was discharged on 11th September 1939, after an uneventful recovery. The diagnosis of this case was clinched beyond a doubt by the isolation of Tubercle bacilli (gram negative, acid-fast and alcohol-fast bacilli) in the CSF. (2) From early cases, atypical cases (e.g. non-paralytic forms) and abortive forms of acute anterior poliomyelitis. (3) From cases of Encephalitis or Encephalomyelitis. In favour of the latter two diseases are 1 disturbance of sleep rhythm, 2 cranial nerve palsies, and 3 low CSF cell-counts. (4) From meningism and serous meningitis. Meningism is a state of meningeal irritation observed in diverse clinical states, especially in children, e.g. apical pneumonia, mumps, enteric, cerebral malaria etc. As a rule, meningism is distinguishable from benign lymphocytic meningitis by the demonstration of a casual factor and a normal CSF composition.

In a series of cases of cerebral malaria, studied by me, there were two cases with cerebrospinal reports highly suggestive of benign lymphocytic meningitis. The CSF was under pressure

there was lymphocytic pleocytosis, the protein content was raised and the chlorides slightly diminished, there were signs suggestive of meningeal irritability. On treatment with Quinine (intramuscular injections) there was an immediate response, the patient's condition being restored to normal within 2 or 3 days.

(5) From Allergic or Helminthous meningitis

Case B Last year, I happened to witness a peculiar case of helminthous meningitis. A boy of 10, the son of a peon, was seen in a drowsy condition with fever, extreme cervical rigidity, positive Kernig's and Brudzinski's sign and sluggishly reacting pupils. The deep reflexes were unduly brisk and the plantar on the right side was extensor. The CSF was under pressure, there were over 50 cells per c mm, all lymphocytes. In view of a past history of round-worms, the boy was given Santonin powder on two successive nights. Within 48 hours of commencement of the treatment, he was restored to a perfectly normal state and the CSF was under normal tension with only about 5 to 7 cells (lymphocytes) per c mm.

(6) Cases of uncertain aetiology. Cases are occasionally encountered in practice with CSF pictures typical of benign lymphocytic meningitis but with clinical pictures so atypical or anomalous that they cannot be classified into any particular category. Whether they are cases of Encephalitis, of acute poliomyelitis or benign lymphocytic meningitis, one is not in a position to say. It is possible that they represent a distinct neurological entity which has escaped the attention of the medical profession, perhaps a new member of the group of "lymphocytic meningeal reactions". From a short acquaintance with cases of this sort I have gained the following impressions:—

(A) Cases usually occur in middle-life. (B) Motor and sensory manifestations are particularly frequent. A common symptom complained of is a feeling of tingling or numbness all over the body. (C) Speech disturbances are common. (D) Meningeal irritability is present. (E) The CSF cell count is usually on the low side, from 10 to 50 cells (usually lymphocytes) per c mm. (F) Sugar and chloride contents of the CSF show little or no alteration from normal. The following Case Report is cited as a typical example of this form of neurological entity—

A Hindoo male, aged 45, farmer, was seen in January, 1940 with a fifteen-days' history of difficulty in walking, tingling and numbness all over the body, severe headache and continuous

fever For the last few days he had lost his powers of speech and had some sphincter disturbance On examination, besides signs of meningeal irritability, there was coarse nystagmus on looking to the right side, the pupils were normal equal and reacted well to light, the cranial nerves were normal and there was increased muscle-tone all over the body, touch pain and temperature sense, vibration sense and joint sense appeared lost all over the body (? functional), the plantars were flexor
W B C was 6400

C S F Report Fluid clear, 16 cells, all lymphocytes, per c mm, protein 0.1 per cent, globulin increased, sugar normal, Bacteria nil

Within 9 days, he made a complete recovery and went home walking

There is no doubt that, with more thorough investigation on the part of the laboratory, we can hope to arrive at a correct diagnosis in the great majority of cases of this sort. Mistakes in diagnosis are due, not so much to ignorance, as to lack of proper investigation for the correct diagnosis of benign lymphocytic meningitis. I would urge a more frequent trial of the following tests for investigations: (1) *The chloride content of the C S F* Very low figures, e.g., below 580 mg are seldom attained in benign lymphocytic meningitis, this serves to distinguish the disease from Tb meningitis. (2) *The glucose content of the C S F* According to Oelsnitz, a normal or almost normal glucose content in a case of meningitis weighs strongly in favour of benign lymphocytic meningitis. (3) *The Tryptophane test* is said to distinguish benign lymphocytic meningitis from Tb meningitis, it is positive in the latter disease. (4) *Repeated examinations of the C S F by Smear, culture and animal inoculation*, should be carried out for the presence of tubercle bacilli, before labelling the disease as benign lymphocytic meningitis. (5) *Animal Inoculation Tests*, e.g., *The Mouse Test of Scott and Rivers*. If positive, it is pathognomonic of benign lymphocytic meningitis. The technique of this has lately been standardized by Scott and Rivers—0.33 cc of C S F from the patient is injected intracerebrally into each of 6 mice within 2 hours of withdrawal. In the event of the patient being a case of benign lymphocytic meningitis, the inoculated animal will display a characteristic clinical picture, usually on the sixth day. The mice with eyes half-closed, sit quietly in a corner of the cage and exhi-

bit dirty, ruffled or staring coats, when stimulated they develop peculiar coarse tremors all over the body with rigidity and extension of the hind limbs. After death, they exhibit congestion and round celled infiltration of the meninges and choroid plexuses. An emulsion may be prepared from the infected brains of the mice and the disease transmitted by intracerebral inoculation through several batches of mice.

(6) *The Serum Virus Protection Test* (or the "Neutralization Test") This test serves to provide immunological proof of the disease by detecting the presence of "neutralizing antibodies" in the patient's serum. A suitable method for carrying out this test has been perfected by Scott and Rivers¹¹

From an emulsion of infected guinea-pig brain a series of dilutions (ranging for 10^1 to 10^3) of the benign lymphocytic meningitis virus are prepared. 0.25 c.c. of each dilution is mixed with an equal quantity of the patient's serum and allowed to stand for 6 hours. Each mixture is inoculated into four guinea-pigs, the test is considered "positive" if 4 or 3 of the four guinea-pigs survive for 18 days.

Summary

Twelve cases of Benign Lymphocytic Meningitis collected from the files of the KEM Hospital during the last five years, are reported and discussed. Our present day views on the subject of Benign Lymphocytic Meningitis are briefly presented and the question of diagnosis fully discussed. In the section on Differential Diagnosis, records are presented of unusual cases of "Tuberculous meningitis with recovery" and "Helminthous meningitis."

My thanks are due to the Dean of the KEM Hospital, Bombay and to the Honorary Members of the Staff of the KEM Hospital, for kind permission to publish notes of cases under their care.

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Case Reports

MULTIPLE LUNG ABSCESSSES

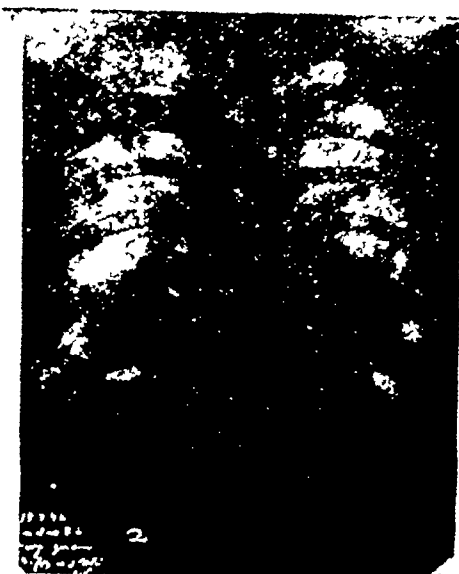
By

N D PATEL

M D (LOND), M R C P (LOND), F C P S

BOMBAY

K J male, aged 35, was seen by me on June 27, 1942 in consultation. He was said to have a continuous fever for a fortnight and was being treated for Enteric Fever. I found no physical signs except a temperature of 102°F, pulse rate 100, respiration 20, spleen not palpable, a clean tongue, and a few scattered rhonchi in the chest, both sides, front and back. He looked rather weak, disinclined to talk and very despondent. He was removed to the Bhatia General Hospital, where the blood examination showed Red Blood Cells 4.71 mil per cmm, Haemoglobin 80 per cent, White Blood Cells 18,000 per cmm, with 73% polymorphs, 1% eosinophils, 25% lymphocytes and 1% large monocytes. The urine and stools did not show any abnormality. Sputum was scanty and showed no Koch's bacilli. The Widal Reaction for B. Typhosus and paratyphoid A and B was negative. The blood repeated next day (28-6-42) also showed a high leucocytic count of 18,000 per cmm. This, with the chest signs, suggested some pulmonary trouble and an x-ray plate of the chest was taken (29-6-42, Fig 1). This did not show any abnormality except enlarged hilar glands and some shadow near the left border of the heart. The physical examination of the chest was also negative, except for the rhonchi. The temperature varied between 100°6 and 97°2 till 3rd July. From 4th to 12th July the temperature remained normal between 99° and 97°F. During this period he was given sulphapyridine by mouth and sodium cacodylate injections. His general condition improved but the high white blood count still persisted. On the 13th July his temperature rose to 100° and on the 14th to 103°F, after remaining practically normal for 10 days. The physical examination of the chest now showed areas of dullness and rales and rhonchi, both sides, front and back. The x-ray taken on the 18-7-42 (Fig 2) showed diffuse areas of consolidation in both lungs, more marked at the bases. He developed persistent exhausting cough, pain in the chest, occasional vomiting and great weakness. The temperature began to swing between 97° and 104°F, sulphapyridine had no effect on it. On the 26th July, i.e., about 15 days after the second rise in temperature he began to show early



- fig 1—Appearance of the chest on admission (20 6 42) to the hospital. Practically negative except for the enlarged hilar shadows
- fig 2—Appearance of the chest after about 3 weeks (18 7 42). There are multiple areas of consolidation in both lungs. No evidence of breaking down anywhere
- fig 3—Appearance of the chest 2 weeks later (1 8 42). Multiple abscesses can be seen very well. It is possible to count eight distinct fluid levels and airspaces, five on the right side and three on the left
- fig 4—Appearance of the chest 16 days later, (17 8 42) showing all the previous abscesses and two more at the right apex with a fresh area of consolidation there

signs of clubbing of fingers and toes. Red blood cells and haemoglobin began to fall, the white blood cells remained high, 20,000 per cmm. An x-ray plate taken on 1-8-42 (Fig 3) shows multiple abscesses. The reproduction printed here has not come out well because of its small size, but in the original negative it is possible to count eight abscesses in all, five in the right lung and three in the left, of these the ones at the bases of both lungs being the largest. Now he began to cough up a considerable amount of sputum every day, which showed all the characters of sputum from pulmonary abscess. The physical examination of the chest showed signs of cavitation. The huge cavity at the left base (front) obliterated the cardiac dullness and gave a suspicion of a pneumothorax. The general condition deteriorated, RBC and Hb falling to 2.3 mil and 55%. The clubbing became drumstick type and well marked and he developed puffiness of face and oedema of the legs. All the treatment given—shortwave therapy for fifteen days, daily glucose, redoxon and sodium benzoate injections, emetine, sodium cacodylate and N.A.B.—was of no avail. The x-ray taken on 17-8-1942 shows all the previous abscesses and *two more* at the right apex. The patient got tired of our treatment and took discharge to try the benefits of Ayurvedic medicine.

Pulmonary abscesses are very frequent in Bombay, some following pneumonia, operations on the nasopharynx, foreign bodies in the lungs, and some so-called primary, but the writer has not seen such multiple abscesses following an illness of so-called typhoid fever. Pulmonary abscesses complicating typhoid fever are recorded in literature before 1880 when *B. typhosus* was isolated and a few since that time, proved by the culture of *B. typhosus* from the sputum. In this case the Widal reaction was negative and unfortunately it was not possible to make a culture from the sputum. It is difficult to decide whether the fever the patient had for a fortnight, i.e., 4 weeks before the lung trouble, was due to typhoid infection or due to pneumonia, though from the description given by the patient, and the treating doctor, it appeared like a mild type of enteric fever.

The four* cases recorded in literature where pure *Eberthella* organisms were cultured from the sputum had all a history of fever for a few days with malaise and chills, three or four weeks prior to the lung complication, the original infection being a mild or ambulatory form of enteric. In all these cases the abscesses were single and small. The abscesses recorded here are multiple and some huge, involving the whole lobes. It is reasonable to assume that they were due to some primary pulmonary lesion or due to septic emboli from some site, which it was not possible to ascertain.

* Bosch (1915) Chunt (1932) Thumm (1931) Harvill (1942) J A Med Assn June 6 1942, 119 p 494

17-7-'42 Non-Protein nitrogen came down to 26.3 mgms/100 cc of blood

23-7-'42 Intravenous pyelography was done and the shadow that appeared to be a calculus in left ureter in a plain skiagram was outside the left ureter. Both the kidneys were functioning normally. This proved beyond doubt that anuria was due to sulphapyridine.

27-7-'42 Patient passed about 50 ozs of urine every day. Urea percentage in urine rose to 1.1%.

Treatment of Acute Suppression of Urine

In order to avoid this complication as far as possible during the administration of this drug, it is very essential to maintain a sufficiently high intake of fluid—five pints or more per day, to prevent the massive crystal formation. The urinary output should also be free, about 2-3 pints or more per day. Urine should be examined daily for crystals and blood. The drug should be discontinued and intravenous fluids be administered with the first appearance of lumbar pain or bloody urine. By taking all these precautions, the danger from renal complications will be reduced to a minimum.

In this case, the patient was given large doses of alkalis by mouth and was encouraged to drink copious fluids. He was given 50 cc of 50% Glucose and one pint of 5% Glucose-Saline intravenously by drip method. In addition, simple measures like fomentations, simple enema and dry cupping on both the sides in the loins were tried without any effect. In the evening on 6-7-'42, he was given one pint of 4.2% Sodium Sulphate solution intravenously and this was repeated every day morning and evening unto 10-7-'42. Symptomatic treatment was carried out for distension of abdomen, constipation and vomiting. Diuresis started on 9-7-'42 and after this the progress was uneventful.

J. M. Rogan and E. K. Cruickshank have successfully treated a case of Sulphapyridine Anuria with Inductotherm (short wave) treatment. Patient passed about 6.8 ozs of urine about an hour after the termination of each of the three applications given within a period of about five hours. Rationale of this treatment is based on the assumption that "the renal tubules are blocked with sulphapyridine crystals, and inductotherm (short wave) treatment is employed with the aim of promoting active hyperaemia of glomeruli and increasing secretion. Thus this therapy may be of considerable value in the treatment of cases, in which the condition is due primarily to mechanical obstruction of the renal tubules. It is unlikely that this treatment would be equally effective, when glomerular damage is present."

It has been said that drugs with a sulphur radicle, magnesium sulphate, sodium sulphate etc., and articles of diet containing sulphur like eggs, onions, cauliflower etc., should not be given to a pa-

tient who is receiving sulphapyridine. The objection raised seems to be theoretical rather than real. In this case, patient, who had already received 15 gms of sulphapyridine was treated for its toxic manifestations by intravenous sodium sulphate solution with very encouraging results.

E J R Smith has treated thirty casualties from France and Belgium with sulphapyridine. To these patients, pentothal sodium, containing 12% sulphur was administered as an anaesthetic by intravenous route. These patients were given sulphapyridine intravenously or by mouth during the operation or following the operation without any harmful effects. Some of these patients were getting sulphapyridine before operation also.

D V Hague has given eggs freely in the diet while treating his cases with full dosage of sulphapyridine without any ill-effects.

Summary

Mention has been made about the toxic effects of Sulphonamide group of drugs.

A case of acute suppression of urine after the administration of sulphapyridine to a patient suffering from pneumonia has been described. He recovered completely with intravenous injection of sodium sulphate (4.2%).

Reference has been given of a case treated successfully with short-wave therapy.

Objection raised in giving sulphur containing articles of food and drugs during the treatment with sulphonamide group of drugs appears to be theoretical.

(My thanks are due to the Dean, K E M Hospital, Dr N K Sahar and Dr J C Patel, in allowing me to report this case, and the latter for many helpful suggestions.)

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A SHORT NOTE ON THE FIFTH ADDENDUM May (1942) TO THE B.P. 1932

By

C. C. MERCHANT

M B B S

(From Pharmacology Dept., Seth G. S. Med. College, Bombay)

The Fifth Addendum to the British Pharmacopoeia 1932 has been published and since "A Review of the Fourth Addendum to the B.P. 1932" was published in the *Indian Physician* (August 1942, page 401), some details as to monographs dealing with the newer preparations as well as important changes in the existing monographs, contained in the latest addendum have been obtained. In the main, the new Addendum may be regarded as an effort directed towards saving of alcohol, and it contains monographs which provide formulae for concentrated preparations to be used as alternatives to the corresponding preparations of the 1932 B.P.

Another noticeable change in the new Addendum is the substitution of Indian Belladonna (*Atropa lutescens*) for the so far official *Atropa Belladonna*, for the manufacture of the official Belladonna preparations. This change was found inevitable because of the impossibility of obtaining *Atropa Belladonna* from the pre-war European sources. The Indian variety of Belladonna is abundantly available and its alkaloidal contents have been found to approach very nearly those present in the European variety, viz., 0.15% in the leaf and 0.25% in the root calculated as Hyoscyamine. The alkaloidal strengths of the preparations, namely liquid extract, liniment and tincture, made from the Indian variety remain the same as before.

As said before, the main feature of the new Addendum is the inclusion of a number of concentrated preparations, to replace the corresponding ones contained in B.P. 1932. These preparations with their doses are as given below—

1 *Liquor Ammoniae Aromaticus*—It is a non-alcoholic solution of ammonia and ammonium carbonate, present in the same proportions as in aromatic spirit of ammonia (B.P. 1932), which the newer preparation is intended to replace in dispensing practice. Doses, however, remain the same.

2 *Emulsio Chloroformi* and

3 *Emulsio Menthae Piperatae*

These preparations replace the corresponding spirits and are o/w type emulsions of chloroform and peppermint oil respectively made by means of liquid Extract of Quillaia. A dose of 1½-3 minims is specified.

4 *Extractum Scillae Liquidum*—In its preparation, the use of Indian Squill has been recommended. Its dose is specified as 2-8 minims.

5 *Liquor Aethylis Concentratus*—It is a concentrated solution of Ethyl Nitrite and is intended to replace the traditional sweet spirit of nitre (Sp. Atheris Nitrosi B P 1932). It is about eight times the strength of the spirit in ethyl nitrite which should be present in freshly made preparations between 17 and 20% and not less than 10% after storage and when the container has been opened occasionally.

Its dose is 2-8 minims.

6 *Eleven Concentrated Tinctures* are included and the methods of their manufacture are described in this addendum. They with their corresponding doses are as follows —

i	Tinctura Aurantii	8 15 min
ii	Capsici	1-4 min
iii	Cardamomi Composita	8 15 min
iv	Cinchonae Composita	8 15 min
v	Gentianae Composita	8 15 min
vi	Limonis	8 15 min
vii	Lobeliae Aetheris	1½ 4 min
viii	Opii Camphorata	4 8 min
ix	Quassiae	8 15 min
x	Tolutana	8 15 min
xi	Valerianae Ammoniata	8 15 min

All the above tinctures are four times the strength of the corresponding tinctures of the B P 1932 with one exception, viz, concentrated camphorated tincture of opium which is approximately eight times the strength of the corresponding older tincture.

Besides, a few minor additions and alterations have been made in the monographs, but they pertain more to the pharmacist than to the physician.

Critical Notes and Abstracts

ANURIA FOLLOWING SULPHADIAZINE THERAPY

Schulte et al report (J A M A May 30, 1942, p 411) a case of acute urinary suppression following sulphadiazine therapy, with recovery. Haematuria, abdominal and flank pain and decreasing urinary output are the symptoms of impending urinary suppression. The treatment suggested is forcing fluids and alkalizing the urine. If the urinary output decreases considerably, cystoscopy, ureteral catheterization and lavage are immediately indicated, with continuous urinary drainage by means of indwelling ureteral and bladder catheters. Subsequently the renal pelvis should be irrigated with 2 per cent sodium bicarbonate solution every three to four hours. Catheters are removed when the urinary output has returned to normal. The authors consider the obstruction to be mechanical.

Hellwig and Reed describe (J A M A June 13, 1942, p 561) a case of fatal anuria following sulphadiazine therapy for broncho-pneumonia. In all he had 24 gms of the drug. In spite of the usual treatment and the ureteral catheterization and lavage of the pelvis, the patient died ten days after the sulphadiazine therapy had been started and twenty-six hours it had been discontinued.

At necropsy, the anatomical changes found were bilateral broncho-pneumonia, subacute pericarditis, focal necrosis of liver parenchyma, large spleen, severe degeneration of the epithelium of the convoluted tubules and ascending limbs of Henle's loop, dilatation of the terminal portion of the collecting tubules, and sulphadiazine concretions in the renal pelvis, haemorrhagic pyelitis and ureteritis.

The anatomical and histological changes are found in acute renal poisoning and cannot be explained on the basis of mechanical obstruction of the urinary passage. The observations of this case and Antopol, and others, suggest that the sulphonamide group of drugs can cause anuria not from degeneration of the epithelium permitting passive diffusion, but from obstruction of the urinary passage.

Careful attention to these drugs appears to prevent renal failure.

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Sodium bicarbonate in *amounts sufficient* to alkalize the urine should be administered simultaneously with sulphonamide drugs

L I I

LOCAL USE OF SULFANILAMIDE IN WAR WOUNDS

Every American soldier who goes into a theatre of war will be equipped with 12 sulfanilamide tablets in a special spill proof metal box as a standard equipment of all troops in combat areas. Medical officers attached to units are to instruct the soldier in the proper use of the tablets. The experience in this war already has demonstrated the efficacy of the drug under war conditions.

SULFANILAMIDE COMPOUNDS IN CLOSED WOUNDS

Frederic W Taylor writes on the misuse of Sulfonamide Compounds (Jour Am Med Assoc, March 21, 1942, p 959) in closed wounds. His conclusions are

1 All common sulfonamide drugs are irritant to tissues when placed in them in powdered form

2 The amount of inflammatory reaction which the individual drugs cause is variable. Some are caustic enough to produce actual abscess. All produce an inflammatory reaction.

3 The practice of placing one of these chemical irritants in a clean benign wound is not justified. It seems doubtful that any drug which produces so much damage to tissue cells could possibly be of sufficient value to warrant its use.

4 The implantations of a sulfonamide powder at the site of an appendectomy is also questioned. This practice cannot elevate the concentration of the drug at a distant peritoneal pus pocket above that obtainable by systemic administration.

5 Adhesions may result from application to bare peritoneum.

6 These procedures give the surgeon a false sense of security, to the detriment of sound surgical judgment.

7 This criticism is not in any way directed against the local or systemic use of the sulfonamides in ulcerations or in contaminated wounds which are left open. The same is true of the systemic use of these drugs in cases of severe peritonitis.

Ferguson criticises Taylor's paper (J.A.M.A. April 25, 1942, p 1514) and gives his clinical experience as regards the usefulness of these drugs. He writes

"I agree with Dr Taylor in his suggestion that the use of sulfonamides locally is unnecessary in routine incisions which are made for clean operations. On the other hand, I am of the opinion that the local use of these drugs, especially the microsulfathiazole

preparation, in contaminated wounds and the traumatic lesions offers the maximum of protection against infection. Sulfathiazole is of more value than sulfanilamide in this respect in that it remains in the wound for a longer period and so exerts a longer action (three to four days). Furthermore, its effectiveness seems to be greater against a wider range of organisms than that of the more soluble sulfanilamide."

L I I

ADHESIONS AND INTESTINAL OBSTRUCTION AFTER INTRAPERITONEAL USE OF SULFATHIAZOLE

Sutton describes the case of a boy (*JAMA* June 13, 1942, p. 559) who was operated on for gangrenous appendix, and 3 gm of sulfathiazole crystals were sprinkled on the peritoneum covering the cecum and ileum where the exudate had been abundant. A month after his discharge from the hospital he began to have attacks of severe abdominal cramps which persisted till December 14, when he had a severe attack of pain with vomiting and visible peristalsis. A diagnosis of intestinal obstruction was made and he was operated on immediately. A loop of ileum was found bound down to the parietal peritoneum posterior to the cecum. This produced a sharp kink with obstruction. The omentum was also firmly adherent at several points to the parietal peritoneum, the ileum and the cecum. The area corresponded exactly with the distribution of the crystalline sulfathiazole. The adhesions were free and the boy made an uneventful recovery. There is evidence that sulfathiazole produces peritoneal irritation in the dog, while sodium sulfathiazole produces dense peritoneal adhesions in the same animal. It seems reasonable to suppose that the excessive production of fibrous tissue both in the wound and on the peritoneum with its attendant complication was caused by an unusual tissue response to sulfathiazole.

L I I

SULFANILAMIDE IN PLEURAL CAVITY

Burford and Graham have used sulfanilamide crystals in the pleural cavity after intrathoracic operations. They use 2 to 15 gm of the drug according to the size of the patient and the degree of the suppuration, and the extent of the contamination. Their results were satisfactory and they state that the local use of the drug is indicated when the contamination of the pleura is extensive. The local implantation of the drug provides a bacteriostatic media at the point of least resistance. The authors tested each candidate with a trial dose of the drug. They saw no ill effect from the local use of the crystals into the pleural cavity.

L I I

SULFATHIAZOLE OINTMENT IN CUTANEOUS INFECTIONS

Kennedy et al (*JAMA* Oct 25, 1941, Vol 117, No 17, p 1415) have used Sulfathiazole ointment in the treatment of cutaneous

infections A 5 per cent sulfathiazole ointment was prepared by suspending finely powdered sulfathiazole, which had been sifted also through bolting cloth to remove large crystals, into equal parts of hydrous wool fat and vanishing cream

Sulfathiazole ointment was used in the treatment of 69 patients with various cutaneous infections It appeared to be efficacious in the treatment of *infected infantile and adult eczema, seborrheic dermatitis, impetigo, acne vulgaris, bacterial folliculitis, and furunculosis*

No toxic effects were observed In 6 of the 8 infants that received applications over one half of the body surface three times a day the concentration of sulfathiazole in the blood ranged from 2.0 to 3.5 mg per hundred cubic centimeters The children and adults that received applications of sulfathiazole ointment over localized areas of the body did not absorb sufficient sulfathiazole to produce a detectable quantity in the blood, although the ointment was applied at frequent intervals throughout the day for prolonged periods

A number of the children with infantile eczema became re-infected when a 5 per cent carbonis detergens ointment was substituted for the sulfathiazole ointment Sulfathiazole was then incorporated in the carbonis detergens ointment, with definite and persistent improvement in the eczema and in the infection

Thirty-five patients with acute vesicular poison ivy dermatitis, 33 patients with cuts and 4 patients with small second degree burns received local applications of sulfathiazole ointment The lesions in each patient healed without infection

SULFATHIAZOLE IN IMPETIGO CONTAGIOSA

Winer and Starkosch (JAMA Jan 17, 1942, p 221) have used sulfathiazole in cases of Impetigo Contagiosa both locally as a 5 per cent ointment in cod liver oil, and orally and have recorded comparative results When used locally as an ointment (Sulfathiazole 1.5 Gm, Cod Liver Oil 7.5 Gm, Hydrous wool fat 4 Gm, Petroleum to 30 Gm) they found on an average 1 oz of the ointment sufficient to cure most cases The average period of cure was 4 to 5 days When used orally, without any local treatment, they gave 1.5 Gm daily to children above the age of 6, and found that the period of cure was practically double—i.e., 9 to 10 days

SULFANILAMIDE DRUGS IN SINUSITIS

L I I

(JAMA Jan 10, 1942, p 181) There is little evidence that a 1 per cent solution of sulfanilamide in physiologic solution of sodium chloride or that a 5 per cent solution of azosulfamide is of value as a spray or as an irrigating solution in the treatment of sinusitis It is not likely that either solution would be irritating

ADRENALINE SUSPENSIONS

In the immediate treatment of acute bronchial asthma, no therapeutic agent has been found which entirely replaces the injection of adrenaline. The absorption and destruction of this drug are, however, so rapid that its effects are brief and difficult to control. Kennedy (*Lancet*, 1941, p 279) describes a method of administering adrenaline which renders its liberation into the circulation as slow as possible, and its rate of absorption as even as possible, during the period of its action. It was decided to associate the adrenaline with ascorbic acid and it was found that actual combination took place. Ascorbic acid considerably retards the oxidation of adrenaline, both in solution and in suspension. When present in excess it keeps the suspension sufficiently acid to discourage oxidation, which does not take place in adrenaline solutions more acid than pH 3. Ascorbic acid is, moreover, non-toxic and favourable results have been described from its independent use in asthma. The suspension finally decided upon was —

Adrenaline base (in very fine powder)	0.010 gm
Ascorbic acid (in very fine powder)	0.015 gm
White wax	0.020 gm
Wool fat (anhydrous)	0.010 gm
Arachis oil B. P.	1 cc

The white wax and wool fat, with a little of the arachis oil are sterilized at 150° C for an hour in a hot air oven and allowed to cool, the rest of the oil being sterilized separately in a similar manner. The wool fat must be anhydrous, and the use of lanolin in one sample led to very rapid absorption and alarming symptoms of overdose. The adrenaline and ascorbic acid are ground to a fine powder in a previously sterilized mortar under aseptic conditions, and are then triturated with some of the cooled arachis oil, the mixture of wool fat, wax and oil is added to form an homogeneous suspension. This is at once transferred to dark ambered glass vaccine bottles, each of which contains 3 cc of glass beads and is filled only half full to allow for shaking. All are then thoroughly shaken. Patients can be taught to give their own injection into the region 2 inches below the crest of the ilium, using alternate sides, and moving backwards 1½ inches with each injection. The average dose is 0.3 cc (i.e., 3 mg of adrenaline base). Its effects are comparable to those of a series of injections of 0.5 cc of 1% adrenaline hydrochloride, and last from six to eight hours.

L I I

DEATH AFTER MORPHIA IN BRONCHIAL ASTHMA

Death from uncomplicated attack of asthma is very unusual. Even from status asthmaticus most patients recover if they are properly handled. The danger of using morphia or other opium preparations during an attack of asthma or during status asthmaticus is well recognised, and almost every practitioner can remember cases

where the use of morphia was followed by sleep from which the patient did not wake up. This fact should be more widely known and practitioners should never use morphia during an attack of asthma, even when other measures fail to relieve the spasm. W T. Vaughan and W R Graham record (Jour Am Med Assoc June 13, '42, Vol 119, No 7, p 556) several cases of asthma which ended fatally within a short time after the use of morphia or dilaudid. They state that the administration of opiates for severe asthma is definitely contra-indicated on two counts. *First*, with the person fighting for his breath and trying to get enough air to prevent anoxia, a drug which depresses the central nervous system, including the respiratory centre, increases the difficulty. *Second*, morphia exerts a slight but definite bronchospastic effect. This is precisely what one is trying to avoid in the treatment of asthma. Again, some asthmatics are sensitised to the opiates and do not tolerate them at all. The authors also warn against the use of supplementary drugs such as digitalis on the expectation that there may be "heart-strain". If there is a definite congestive cardiac failure, digitalis may be used, otherwise its use is not warranted. To use it when the heart is of normal size and tone, is to further contract and diminish the output, which will only impair the oxygen delivery to the tissues, and aggravate the state which is already anoxicemic.

L I I

RUPTURED INTERVERTEBRAL DISCS

On a discussion on Sciatic Pain before the joint meeting of the sections of Neurology and Orthopaedics this subject was touched by several speakers (Proc Royal Soc Med Vol XXXV, May 1942, p 505). Joe Pennybacked stated that the majority of the cases of sciatica were due to compression of one of the lower lumbar roots by a damaged intervertebral disc. He had verified this lesion at operation in sixty cases in the past two and a half years. In every case of sciatica the possibility of a prolapsed disc must be remembered. The diagnosis can often be made from the history. The lesion is traumatic. The injury is usually trivial and often forgotten. The injury or strain commonly recurs in flexion of the trunk, in lifting from the bending position, for instance. The immediate damage to the disc is followed by *low back pain* often miscalled lumbago. This pain may be severe and disabling for a few days or it may cause only a slight discomfort in the back. The neurological examination reveals pain on the straight-leg raising test, some tenderness over the course of the sciatic nerve, weakness of the muscles below the knee, a diminished or absent ankle jerk, and slight sensory impairment over the lateral border of the foot and ankle. Not all of the signs are present in every case. The C S F is normal, except in cases of massive protrusions causing compression of the cauda equina, where there may be a great increase of protein. The x-rays of the spine are of little help. They

show in-flattening of the lumbar curve and scoliosis. Myelography with lipiodol or air may demonstrate some cases but should be avoided and the diagnosis should be made from the clinical history and examination alone. An explorative operation is advisable to contrast myelography.

C P Symonds, the neurologist, said that he had observed scores of cases of prolapsed disc who had recovered with warmth and rest and without surgical intervention. He thought that the lesion was capable of spontaneous repair. In the service patients, prolapsed disc was by far the commonest cause of sciatica. The clinical syndrome of prolapsed disc was characteristic and the diagnosis could be made without contrast media. He was not yet convinced that operation offered a short cut to recovery or that the prospects of recurrence were any less in cases treated by operation than in medically treated cases.

Walter E Dandy records six cases with serious complications of the Ruptured Intervertebral Discs (Jour Am Med Assoc June 6, 1942, Vol 119, No 6, p 474). Of these six cases one was cervical, one was thoracic, and four with lumbar discs. The rupture of the cervical and thoracic discs had disastrous results—total paralysis and death from pressure, necrosis of the spinal cord in the former, and in the latter the paralysis cleared only partly. The rupture of the lumbar disc caused in one case permanent sensory paralysis in addition to long continued pain and loss of bladder function with subsequent infection of the urinary system. In two other lumbar cases there was complete paraplegia and loss of bladder function and in the fourth lumbar case there was long continued bladder incontinence and infection. These six complications occurred in a series of 300 operative cases, a percentage of 2. All these sequelae could have been prevented with early diagnosis and treatment. Dandy considers spontaneous cure of ruptured disc infrequent and a high percentage of permanent cures only after an operation. After the spinal cord is involved operative treatment within a few hours is imperative if any function referable to spinal cord is to be expected. Iodized oil is indicated for an early diagnosis when the spinal cord is involved, i.e., when the rupture is in the cervical or the thoracic region. It is not indicated for rupture of a lumbar disc because with rare exceptions the diagnosis can be made with much more accuracy and certainty without it.

L I I

LUMBAR PUNCTURE

The occurrence of headache during the ensuing one to three days after the lumbar puncture is well known to everyone. It is also recognised that the presence of space-occupying lesions within the cranial cavity as suggested either by the history or by the physical findings including an examination of the optic discs, con-

stitutes a definite contraindication to its use Munio and Harding (Jour Am Med Assoc June 6, 1942, p 482) suggest the potential role of the Lumbar Puncture in the production of injuries to the intervertebral discs The intervertebral disc is composed of two distinct parts, the annulus fibrosus and the nucleus pulposus The mobility of the spinal column as regards flexion, extension, and rotation is dependent on the plasticity of the discs Any injury to the annulus fibrosus, whether resulting from excessive stretching or from direct penetration, can be expected to permit the protrusion of the plastic nucleus beyond the limits of the borders of the vertebral bodies Anteriorly or laterally such a protrusion will cause few significant symptoms, but posterior protrusion will encroach on the vertebral canal and distort the spinal roots, as they enter the intervertebral foramina and produce subjective or objective signs The greatest strain on the posterior ligaments is at the 4th and 5th lumbar and 1st sacral vertebrae and it is at this point that clinically recognizable herniations of the nucleus pulposus are most frequently found

The occurrence of injury to the annulus and nucleus by the spinal needle during lumbar puncture has been reported by several writers The material from the disc might block the needle (Levinson, 1919), Billington (1924) recorded 35 cases of back pain after lumbar puncture, and Pease (1935) reported evidence of protrusion of the nucleus following lumbar puncture in 12 cases The authors took lateral x-rays of the spine with spinal needles in situ, in consecutive fifty punctures done by members of the staff of the Department of neurosurgery, Boston City Hospital From the study of these they conclude that the custom of approximating the patient's neck and knees as a prerequisite to lumbar puncture is without any anatomical basis and should be abandoned Further, they state that the position of the needle in most cases demonstrates that perforating injury to the posterior part of the annulus fibrosus is a distinct possibility during the course of lumbar punctures done even without forced flexion of the spine and by men familiar with the procedure They also suggest that the interspace between the last lumbar and the first sacral vertebrae is the location of choice and that the spaces between the 3rd and 4th lumbar vertebrae and 4th and 5th lumbar vertebrae should be avoided whenever possible

L I I

HYPERTENSION DUE TO RENAL EMBOLISM

Fishberg records five cases of hypertension due to renal embolism (J A M A, June 13, 1942, Vol 119, No 7, p 551) These observations offer direct clinical evidence that elevation of blood pressure may result from an impediment to the flow of blood through one or both kidneys It appears to present a particularly close analogue in man to the hypertension that Goldblatt (1934) first produced in the dog by the application of his clamp to the renal artery and

This phenomenon they attribute to two separate mechanisms (1) Due to the coexistence of mitral regurgitation which raises the intra-auricular pressure, as a result, a larger amount of blood passes with augmented force into the left ventricle during rapid inflow and causes a marked degree of distension of its walls, (2) due to a decrease in the tonicity of the ventricular musculature, a consequence of rheumatic infection

In other cases of early rheumatic mitral diseases, these authors found that vibrations of the auricular sound occur soon after or together with those of the third sound and serve to enhance the acoustic effect of a rumble Bland, E F, White, P D and Jones, T D *Ame Heart Jour* 10 995 (1935) Jaquiri, A C, Massell B F and Walsh, B J *Ame Heart Jour* 20 295 (1940)

R J V

PREVENTION OF "RETURN ATTACKS" OF RHEUMATIC FEVER

Wasson, V P and Brown, E E *Ame Heart Jour* 20 1 (1940)

This paper deals with the effect on a series of cases of rheumatic fever, of immunization with a "filtrate of N Y S haemolytic streptococcus" From the laborious and systematic data presented by these authors it appears that inoculation with this "filtrate" in patients of rheumatic fever serves to reduce the number of rheumatic fever attacks and hence the incidence of carditis

In a two-year follow-up of rheumatic cases at the Flower-Fifth Avenue Hospital, it was noted that the incidence of rheumatic fever attacks was 7% in the "treated" and 33% (with one death) in the control group The routine procedure with each treated and untreated case was the same, a detailed history, a thorough clinical examination, an exercise tolerance test, a teleroentgenogram, an electrocardiogram, a routine urinalysis, a complete blood count, the sedimentation rate were resorted to in all these cases Though the total number of patients treated with this "immunization method" is too small to allow any definite conclusions, nevertheless the results obtained by these authors are impressive enough to suggest a more extensive trial of this method of prophylactic treatment

R J V

The Indian Physician

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Let us remember

THE APHORISMS OF CORVISART

(Continued from page 464)

CXLV The urine is most often scanty, cloudy, turbid, red, with brickdust sediment. The decrease in this fluid depends upon defective excretion, and not upon any disease of the organs which form it, since autopsy has never demonstrated the slightest lesion no matter to what extent the urine showed abnormality.

CXLVI At the same time as the diminution in the amount of urine there is evident, an infiltration (edema) which begins at first about the malleoli, then in the legs, the thighs, the trunk, the arms, and finally becomes general. This is in proportion as the disease advances. One may say that this infiltration which is consecutive to organic disease of the heart, is in inverse ratio to the ease of respiration, and to the quantity of the urine. This infiltration likewise involves the body cavities developing hydrothorax, ascites, infiltration (edema) of the lungs and in general, all regions of the body.

CXLVII The type of sleep, or rather of insomnia, is also characteristic of this disease. When these patients are about to go to sleep, they are suddenly awakened and aroused, finally being forced to get out of bed to avoid being suffocated. Many of them pass the entire night seated in a chair or at the window. In general they sleep very little, and their sleep when they have it, is in no sense restorative, often being interrupted by disturbing dreams.

CXLIX The symptoms of the disease are all easily explained. The discoloration and injection of the face, or of its parts, comes from stagnation of blood in the capillary system as a result of impeded circulation. The difficulty in respiration comes from pulmonary infiltration, edema, and stasis of blood in the lungs, because of the obstacles which in certain cases, the fluid has to overcome in returning to the heart. In the earlier stages, the respiratory difficulty comes only from this circulatory factor, since pulmonary infiltration and edema do not take place till the disease is well advanced. The forcible pulsation and palpitation of the heart are due to the efforts made by that organ to overcome the obstacles which impede the circulation. The character of the pulse is an exact picture of the condition of the circulation and reveals all its qualities. The decrease in the amount of urine depends upon a default of secretion, which in turn is due to circulatory disturbance. Infiltration edema of the tissues is due to such causes exclusively. Whenever the circulation is impeded, there is edema.

Diagnosis

CLIV We recognize the presence of calcification of the mitral valve, when on placing the hand over the precordium, one feels a sort of thrill, similar to that experienced by the hand while stroking a cat which one is petting. This thrill is produced by the obstruction which is met by the blood coming from the lungs and aortic to enter the left ventricle.

CLXII One must carefully avoid applying the term "heart disease" to every instance of palpitation of that organ. We will easily distinguish this type of condition by the factors which brought on the attack, by its short duration and total cessation as the result of rest, or at most, some mild anti-spasmodic medication. We must be aware, however, that the attack which is purely nervous in origin may, by reason of its frequent repetition, become organic.

CLXIII There are three diseases which have some analogy to heart disease. These are hydro-pericardium, hydrothorax and asthma. Essential primary hydro-pericardium is a very unusual condition. It always presents some of the symptoms of cardiac disease but never the complete symptom-complex. The symptoms which are present are rather milder than those of

actual heart disease Moreover, these do not appear until the pericardium is filled with serous fluid, which will interfere with the usual resonance on percussion The immediate precipitating causes of the two conditions are also quite different

Hydrothorax presents almost the same distinctions Moreover, one will notice that respiratory difficulty begins only after the pleural effusion has accumulated, a condition easily recognised by percussion On the other hand, in heart disease, respiratory embarrassment is present at a period when the entire chest is still quite resonant Percussion, therefore, is especially valuable in demonstrating the marked difference between these two diseases

As to asthma—this is a periodic disease, the paroxysms of which last only a few days It is influenced by atmospheric conditions, etc All of its peculiarities distinguish it definitely from disease of the heart If, to this, we add the assistance of percussion, there is no excuse for error

Prognosis

CLXIV All diseases of the heart are incurable and eventually terminate fatally

CLXV However, patients may delay or hasten this outcome to some extent, depending on whether they protect themselves by the most absolute rest, whether they avoid all that is harmful, and to the extent that they employ appropriate remedies

CLXVI The art of medicine is not sufficiently advanced for one to state just which type of organic disease of the heart is most rapidly fatal

CLXVII In proportion as the symptoms are mild, one may hope that the patient has more time to live On the contrary, as these increase in intensity, the closer is the termination of the disease It is especially upon the condition of the respiration and of the circulation, that one should base his prognosis in this respect

CLXVIII One must not allow himself to be misled by apparent success Sometimes, after a more or less extended course of treatment, a patient becomes free of edema, breathes

more easily and even the pulse regains its regularity. We would then tend to consider them as cured. However, after these patients have resumed their work, sometimes on the very day, all of the symptoms return with an intensity in proportion to the duration of the disease. In spite of the relief which one may secure for the patient, the disease continues to progress just the same.

Treatment

CLXIX In view of the prognosis of diseases of the heart, one can appreciate that it is foolish to attempt to cure the lesion. One must limit himself to palliating the symptoms which present themselves with the sole aim of prolonging the life of the patient.

CLXX This disease, during its early stages, or at a period when treatment could possibly cure, causes so little fatigue or distress that patients will not believe they should be alarmed. Consequently they usually seek assistance only when it is too late to cure.

CLXXI Before using any therapeutic measure, it is necessary that the patient be given the most absolute rest for the heart, the body, and the mind. Without this, remedies are useless.

CLXXII When the patients are florid, plethoric, with short, laboured respiration, and a high bounding, hard pulse, we usually make one or two moderate bleedings. If the patient is less vigorous, or the plethora is less marked, one will limit himself to the application of leeches to the anal region. Usually there is considerable relief from this measure, which, however, must be used with much caution for fear of precipitating serious reaction (anaphylactic edema).

CLXXIII We meet this latter condition by the use of aperitives, beginning with the mildest drugs and increasing gradually to the more active. In proportion as these are effective, that is to say, as the amount of urine is increased, one will note that all of the symptoms are alleviated. Not only does the edema decrease under observation, but breathing becomes easier, the pulse shows less deviation from normal, the face is less congested, sleep is more restful, palpitation less disturbing, etc. The patients believe themselves to be cured, but as has been said, it is wrong to accept this idea.

CLXXIV The measures which produce these fortunate results when the disease has not yet reached the most advanced stage, no longer give relief when it has progressed to the final stage, and the patient is overcome by actual suffocation

CLXXV We treat the sharp palpitations by the use of anti-spasmodics, which cannot cure the disease, and which can only bring comfort

CLXXVI When there is severe pain in the precordial region, and patients complain of great oppression, we make local applications, sometimes of a few leeches, sometimes of an emollient ointment, sometimes of a blister, entirely with the idea of confirming the patient in the belief that he is being helped. Nevertheless, blisters do occasionally give considerable comfort though we cannot explain exactly why or how

CLXXVII When the serous diatheses (edema) has so far advanced that it has spread, not only to the surface, but also to the interior of the body, and aperitives do not produce relief promptly through the elimination of urine, one may attempt to secure results by means of purgatives which will give rise to watery stools. This will be of value to the patient

CLXXVIII When one has reason to believe that the disease of the heart is caused by the action of any of the toxins, be it syphilis, psoriasis, rheumatism, etc. or to any other such cause, appropriate specific treatment should be given, that is to say, administer anti-venereal remedies

CLXXIX Opium which has been thought valuable to relieve symptoms and give sleep, is, however, apt to do more harm than good in these diseases

CLXXX Diet should be in proportion to the appetite of the patient, which is usually very good. It has been remarked that some patients are temporarily relieved while eating. Fluids likewise, should be allowed in proportion to the thirst which is sometimes increased

CLXXXVIII Note In these aphorisms we have not spoken of disease of the pericardium. We shall indicate only one form which has all the characteristics of heart disease. It is due to close adhesions between the pericardium and the heart, so

that one is unable to demonstrate whether this membrane is present, or not. One can prove that such a structure is present, however, in spite of the intimate adhesions, by noting that the apex of the heart draws up the diaphragm. This disease of the pericardium is undoubtedly caused by a low-grade inflammation.

Plethoric Conditions of the Blood

CXC We must discount the statements of patients who, during an attack of hemoptysis are convinced they have vomited blood, because they have brought up a large amount at one time and have expectorated it easily.

Pulmonary Phthisis

CXCI One may develop phthisis at any age, one sees this disease from infancy until even the most advanced old age. It is true that middle age is the period at which this disease makes its greatest ravages.

CXCII We understand by "dry phthisis," that form in which the patient does not expectorate. The term should also apply to that form where the patient expectorates only phlegm or saliva. So long as they do not expectorate purulent material, one must speak of "dry phthisis."

CXCIV Nearly all tuberculous patients complain of distress in the stomach. When asked to place their hand over the seat of pain, they indicate the lower and median portion of the thorax. However, we see that the stomach has nothing to do with the matter.

CXCVI Moreover, we know that in emaciation from lack of assimilation, there is always a low-grade fever, while there is none in the form due to starvation.

CXCVII Those patients whose lungs are involved in this disease always show the oldest lesions in the upper lobes.

Laryngeal Phthisis

CXCIX Ulceration of the larynx, or of some of its constituent parts represents the disease which we call laryngeal phthisis.

CCII This form of phthisis very rarely occurs as an independent lesion. It usually complicates pulmonary phthisis.

CCIII When it has reached an advanced stage it is, like the latter form, incurable

CCIV The symptoms of this disease are complete aphonia, a constant pain referred to the larynx, which in turn may present evidence of breaking down. Also to some extent, there are the general symptoms of pulmonary phthisis as emaciation, low-grade fever, etc

The Effusions—Dropsy

CCXII The content of the fluid in edema or dropsy varies greatly. It may be blood-tinged or colorless, tenacious (viscous), watery, icteric, etc

CCXIII In spite of the opposition which certain persons have to mechanical explanations, one must not fail to recognize that sometimes these are correct. For example, in dropsy the fluid, left to the influence of gravity, almost always collects in the most dependent part. All patients with dropsy or anasarca show more edema on the side on which they lie, if they turn over, the serous fluid reaches the other side, it collects in their limbs when they are up and about, etc

CCXIV One of the most valuable characteristics by which we recognize an encysted hydropsy from other forms, is the slowness with which it shifts on moving the patient

CCXV There are many patients with dropsy who have not that excessive thirst of which the authorities speak

CCXVII During periods of national poverty and hardship, the hydropsies are the predominating lesions. In the year 1793, three-fourths of the patients who presented themselves at "La Charité" suffered from this disease

Hydrothorax

CCXXIV Percussion, together with other peculiarities of this disease, is the best means we possess of confirming the presence of fluid in the thorax. By employing this procedure from time to time, one may learn whether the disease is increasing or diminishing

CCXXVI Patients suffering with hydrothorax die almost without distress or with the mildest of symptoms. While in the

case of heart disease, which as regards symptoms, has some analogy to this form of hydrothorax, the course is quite different

Ascites

CCXXVII Ascites is a very common disease. One must carefully satisfy himself that it may not depend upon an organic lesion, which can usually be determined by examination. In general one must thoroughly familiarize himself with technique of palpation (examination) because it frequently becomes most valuable.

CCXXVIII When the ascites is due to lesion of some of the organs of the lower abdomen, it usually precedes edema in other parts.

White Swelling (Edema)

CCXXXIV Anasarca or edema caused by disease of the heart or great vessels, begins by an infiltration of the feet which gradually extends to involve the thighs, the abdomen, then the upper extremities, and finally, the body cavities, especially the thorax.

Treatment

CCXXXVI It is quite rare that one is able to cure an anasarca of any considerable extent. It is sometimes possible to reduce the edema, but this usually recurs after a short period.

CCXXXVII One may call into use many therapeutic methods in the treatment of this disease. We may try the following forms of treatment: that of diuretics, that of drastic purges, that of sudorifics, emetics, etc. The first two are usually preferred.

CCXXXIX When medical measures are impotent, we have sought to prolong the life of the patient by surgical operations. For ascites we do paracentesis. One should resort to this measure, only, when respiration is disturbed to a degree threatening suffocation. One need have no fear of the lipo-thymic reaction occurring as a result of this operation, as has been spoken of by various authors. This does not ordinarily occur, in spite of the fact that one has entirely emptied the serous fluid as rapidly as possible. Therefore, it is better to entirely remove the serous fluid at one sitting, than to do it in several attempts.

When the abdomen has been emptied of the ascites, one may then profitably make examinations to discover lesions of the abdominal organs

CCXLI In edema of the extremities we sometimes make scarifications upon the limbs, with the idea of allowing the serous fluid to escape and thus relieve the edema This is sometimes accomplished quite rapidly The method should be used somewhat sparingly, however, although the temperature may be quite moderate, gangrene is liable to occur, which is a most untoward complication The scarifications should be quite small

CCXLII After one has made these sacrifices, the condition of the urine usually improves for several days afterwards This is because the procedure decreases the engorgement of the tissues, which in turn improves the circulation, and as a result there is increased secretion of the urine

Paralysis

CCXLV The closer the paralyzed structures lie to the head, the more difficult is the cure Paralysis of the tongue is most difficult to cure

CCXLVI When a paralyzed extremity regains the power of motion, the part farthest from the head is the first to show improvement

Pertaining to Asthma

CCL Many physicians mistake actual disease of the heart for asthma However, the two diseases are quite different, especially in their course, duration, and termination

Cancers—Pertaining to Cancer of the Stomach

CCLV Cancer of the stomach is a common disease

CCLVI We have to recognize three varieties of this disease cancer of the esophageal orifice, that of the fundus of the stomach, and that of the pylorus

CCLVII The first form is most unusual, the second is next in order of frequency, and third type is most common

CCLXIII In these patients emaciation occurs from lack of nutrition In these cases, one never observes low-grade fever, also the pulse remains very steady throughout the disease.

CCLXV When this disease is well established, it is incurable and fatal Its duration is limited, which serves to distinguish cancer from nervous vomiting which may extend several years

Gilder's Tremor

CCLXXI Gilders and indeed all workers who use mercury are liable to contract a peculiar tremor which we call "gilder's tremor "

CCLXXII This tremor develops in a progressive manner and reaches a point at which the patient is forced to stop all work

Scurvy

CCLXXV There are occasional instances of true scurvy in which the gums are healthy and do not bleed

CCLXXVI In some of the spring fevers, it is rather common to see repeated attacks of nose-bleed and other symptoms of scurvy appear The juices of certain antiscorbutic plants, especially that of sorrel, easily available in this region, are efficient remedies for this condition

CCLXXVII Among the cachectic deteriorations, scurvy is one of the most common The physician must be on the lookout for it, to the end that appropriate remedies may be given

Worms

CCLXXXII In spite of various signs and symptoms which have been described, the demonstration of the presence of worms in the human body is very difficult, and sometimes impossible

Termination of Diseases

CCLXXXVI We know that any disease may end in one of three manners; by changing into a different condition, by death, or by a return to health We shall say nothing concerning the first termination

Death

CCLXXXVIII To say that a patient died suddenly is to say nothing, since many widely different conditions may cause sudden death,

CCLXXXIX The cordials which we give in the terminal stage of all diseases, are in some circumstances, more likely to precipitate the end than they are to retard it

Pertaining to Post-Mortem Examination

CCCVI The aim of all post-mortem examinations being to enlighten oneself concerning the manner of death of the patient, and to be instructed in pathologic anatomy, one should allow no opportunity of making such examination to escape, and should carry it out with the greatest of care. It is the best means of gaining information in medicine and of extending that science

Pertaining to Convalescence

CCCVII The transition from the condition of disease to that of perfect health is called "convalescence." It is a mixed condition during which the systems of the body return little by little to their normal functions

CCCX When they have need of building up, one should allow patients to recover by means of nourishing foods before purging them, should this be necessary. Purgation will weaken them still more and may be harmful rather than beneficial, without this precaution

CCCXIII Patients who have recovered from a very acute disease, or who have been on a rigorous diet, sometimes have a ravenous appetite. If they take it into their heads to satisfy this appetite greedily, they will die quite suddenly, or suffer a relapse of the original disease, which is then more serious. We explain this fact by saying that the stomach, in order to provide for digestion, draws the few remaining vital forces to itself, and then, the individual succumbs

Pertaining to Medicaments

CCCXV We use the term "medicament" referring to measures which the physician uses to combat disease

CCCXVII In order to be assured of the effects of any medicine, one must know that the substances from which it is prepared are of the best quality, that the preparation is accurately and faithfully carried out, that the patient takes it all, and finally, that he follows the prescribed conditions. Except under such circumstances the object of the physician is not

attained In hospitals where these directions are usually indifferently followed, the patients suffer from it and the results are less favourable, all things considered, than in private practice

CCCXVIII Whatever may be the effect of a medicament, provided it is not harmful, its use should be continued over some period, in order that one may judge its effect For if we change because of some slight inconvenience of which the patient complains, it will be necessary to do this repeatedly Such vacillation in these matters of medical practice is very reprehensible

CCCXIX We should doubt any medicine to which too many virtues are attributed, especially if these are opposed to one another

CCCXXI When one is puzzled concerning the treatment to choose for a given patient, one may attain his end by the analytical method One reviews the various procedure of efficacious medical practice, such as bleeding, emetics, purgatives, blisters, etc One considers the indications and contraindications of each If after this deliberation, one cannot make up his mind to use any of these, he concludes that it is best to practice expectant medicine, that is to say, he will limit himself to general methods, at least until new indications present themselves

Original Contributions

THE DIAGNOSIS OF GASTRIC DISORDERS

The gastric symptoms are the most frequent complaints of the patients in the out-patient department of the general hospitals as well as in the consulting room. Of all these patients only a few suffer from organic disease of the stomach, the rest have disease elsewhere in the body and the gastric symptoms are only reflex manifestations. In a consecutive series of 15,000 patients with chronic dyspepsia examined at the Mayo Clinic, the number of patients with organic lesions were as follows —

18.7	per cent duodenal deformities and niches
1.5	per cent gastric ulcer
0.3	per cent both gastric and duodenal ulcer
<hr/> 16.5	
2.6	per cent gastric carcinoma
<hr/> 18.1	per cent

Thus only about 18 per cent of patients had their digestive disturbances as the result of the commoner, primary, gross, organic disease of the stomach and duodenum. These figures are borne out by other Western observers, but my impression is that for Bombay hospitals and especially for private practice these figures are too high. I do not think that the percentage of gross organic lesion will be higher than ten or even less here.

To diagnose organic disease of the stomach and duodenum, apart from the clinical examination one resorts to fractional test meal, stool examination for occult blood and the roentgenological examination. Of these the last is the most important by which one can diagnose ulcer of the stomach and duodenum, gastric carcinoma, pyloric obstruction, duodenal obstruction, stasis, dilatation, or adhesions, certain forms of gastritis, rare benign granulomas, diverticula and diaphragmatic hernias. These will comprise about 10 per cent of the cases. The remaining x-ray negative cases are indeed a diagnostic problem and often tax the diagnostic ability of the physician to the

maximum. If the x-ray examination is made by an inexperienced, careless, uncritical radiologist, the diagnostic difficulties of the physician are made worse in all negative reports.

It is advisable if the clinical history warrants, to have a second examination by the same radiologist or by some other colleague.

By a careful x-ray examination using the modern technique, it is possible to diagnose approximately 90 per cent of the gross organic lesions of the stomach and duodenum. Ulcers of the stomach and duodenum are not so common in Bombay as they are in the West. The post-mortem room and the operation table show that these lesions are diagnosed more frequently than they should be. The diagnosis is often made on insufficient evidence.

Radiologists say that there are certain organic disorders of the stomach and duodenum which cannot be detected by the x-rays. At least 15 per cent of the duodenal ulcers are said to escape detection unless a special technique is used and about 5 to 10 per cent are said to be impossible to be detected by the radiologists. The same can be said of the small gastric ulcers and small carcinomatous ulcers which do not produce a niche or a filling defect. For these a study of the mucosal relief is necessary. In Bombay no radiologist has studied the various forms of acute and subacute gastritis and it is difficult to say anything about its prevalence here. Small paraoesophageal (hiatal) diaphragmatic hernias are also likely to escape radiological detection.

Of the radiologically negative cases a very large number falls under the group of *Functional Gastric Disorders*. Roughly about 30 per cent of the cases seeking medical advice for stomach trouble are found to suffer from no organic lesions of the stomach and have no organic lesions elsewhere in the body, but suffer from what is known as functional dyspepsia or nervous indigestion. Alvarez has beautifully described this condition in his excellent monograph, "Nervous Indigestion". No practitioner treating gastric disorders should be without it. These patients complain of gastric symptoms for a very long time without any steady deterioration in their health. The symptoms are extremely variable, and show no

A TABLE SHOWING AN APPROXIMATE FREQUENCY OF CAUSES OF GASTRIC DISORDERS

15 per cent	I Organic Diseases
	Ulcer of the stomach and duodenum
	Carcinoma of the stomach
	Pyloric obstruction
	Duodenal obstruction dilatation or stasis
	Adhesions
	Acute and subacute gastritis
	Benign granuloma and lymphomatous tumours
	Diaphragmatic hernias
35 per cent	II Functional Gastric Disorders
	Constitutional inadequacy or habit dyspepsia
	Gastric neuroses or Psychoneuroses
	Gastric allergy
	Gastritis
30 per cent	III Reflex Gastric Disturbances from Diseases of other Abdominal organs
	Diseases of gall-bladder, liver, appendix, pancreas, small bowel, colon, intestinal worms, epigastrics hernia, suprarenal glands, TB peritonitis, tabes mesenterica, diseases of the vertebral column
20 per cent	IV Gastric Disturbances from other Remote Diseases
	Circulatory diseases
	Pulmonary diseases
	Nervous diseases
	Urinary Diseases
	Endocrine diseases
	Deficiency diseases
	Intoxications, eg, lead, alcohol, tobacco, co, drugs, etc

sequence so characteristic of the organic diseases. There is always a history of some emotional disturbance and the symptoms fluctuate with the changes in the emotional tone of the patient. The description of the complaint is often a projection of the patient's psychological state, and varies from patient to patient according to his mental make-up. In most cases the physical disability is marked and is often out of proportion to the severity of the symptoms. The very convincing narration of the symptoms drives many an unwary physician or sur-

geon into a trap and many an operation is performed for gastric or duodenal ulcer, cholecystitis, or appendicitis. A careful examination very often shows other stigmata of psychoneurotic or hysterical personality. A good many of these patients return with frank psychoneurosis after a lapse of years.

Gastric allergy as a cause of chronic gastric complaints is well recognised now. The symptoms may simulate organic disease of the stomach. A history of eczema, asthma, vasomotor rhinitis, migraine, angioneurotic oedema or spastic colon in the patient or in his family should be helpful in the diagnosis. The spasm of the pylorus in this case produces pain which is very much like that of ulcer and is frequently associated with vomiting. The relationship to food should also be helpful because these patients vomit immediately after taking some food which disagrees with them.

Gastritis, in its acute forms, is not difficult to diagnose but about the existence of chronic gastritis, there is always a feeling of doubt. The pain of gastritis is said to simulate gastric ulcer quite well.

Disease of any abdominal viscus is likely to produce motor or secretory disturbances of the stomach. This may be as a result of common innervation or circulatory inter-relationship or common embryological origin. The most important organ in this respect is the *gall-bladder*. Chronic non-calculous cholecystitis or a gall-bladder with stones is responsible for approximately 20% of all cases of dyspepsia. The classical fat, fertile, females of forty or over are well-known subjects of gall-bladder disease. But the gall-bladder disease is equally frequent in fat males and in younger and thinner subjects of both sexes. Epigastric discomfort, gaseous distress, belching and a feeling of fullness are the chief symptoms. The attacks are recurrent. The symptoms come on soon after meals. In the absence of a history of biliary colic or with a negative cholecystographic result, the diagnosis has to be made on clinical history only.

Appendix is less frequently responsible for chronic dyspepsia. In an occasional case, the indigestion improves after removal of the appendix but in most cases, one feels that it is blamed unnecessarily. A diseased appendix is a common accompaniment of chronic disease of the upper abdomen.

Liver diseases such as hepatitis, amoebic or toxic, and cirrhosis, portal or biliary, are often associated with chronic gastritis and chronic indigestion. In early cases of cirrhosis of liver before ascites has occurred the x-ray examination of the oesophagus for the varix may be useful, also tests of hepatic function such as Takata-Ara test, hippuric acid test or icteric index may be helpful. Haematemesis or melæna may be the first sign of cirrhosis.

The diagnosis of the diseases of the *pancreas* is always very difficult. Acute and subacute pancreatitis, chronic pancreatitis, pancreatic calculi, and pancreatic carcinoma are often associated with epigastric pain or dyspepsia. Loss of weight, a palpable mass, changes in the serum lipase, and the indirect evidence showed by the x-ray examination may help in the diagnosis.

Many sufferers from diseases of *small and large bowel* complain of gastric symptoms. Sometimes stomach is involved in the pathology as in case of gastro-enteritis. In other cases, such as partial obstruction of the small bowel, spastic colitis or irritable colon, the stomach symptoms are reflex manifestations. Certain pathological states of the colon, such as carcinoma or ileocaecal tuberculosis or dysenteric ulcerations, are accompanied by pain which needs careful analysis and investigation to differentiate it from the ulcer pain.

Pain of an *epigastric hernia* may simulate visceral disease. The pain is not related to food or exertion. It may be ulcer like in character or only diffuse abdominal cramps.

A variety of abdominal states such as *tubercular peritonitis*, *tabes mesenterica*, or *suprarenal disease* may produce gastric disorders which may give most difficulty in diagnosis. Sometimes caries, osteoarthritis, or metastasis in the lower *thoracic vertebrae* may produce pain which is confused with ulcer pain. Indigestion, abdominal pain, and haemorrhage frequently result from *parasitism* of the upper digestive tract by hookworm, roundworm *Giardia lamblia*, or *Strongyloides stercoralis*. Roundworms have a habit to wander about where least expected and should always be excluded before other diagnosis is made.

Stomach complaints are fairly frequent in a variety of *systemic diseases*, but only rarely the gastric disturbance is the sole

A large number of them had developed both boils and impetigo. The prickly heat improved with application of a dusting powder containing ordinary starch, boric acid and zinc oxide in equal parts twice a day. It finally disappeared with the advent of the monsoon.

Boils —Septic prickly heat and boils were painted with organic dyes (1% solution of gentian violet in alcohol) and when the boil was big enough it was incised. In about 13 cases staphylococcus toxoid helped to ameliorate the severity of the boils, and when they left Bombay for their camp in Jamnagar only 4 of the small children were still suffering from boils. These had not reacted to about 5 injections of graduated doses of staphylococcus toxoid.

Scabies —Only 5 children were infected with scabies. It was treated with success with 10% sulphur ointment, the usual precautions being taken. The small incidence of scabies in this group seems worthy of note.

Impetigo —Sixty-one children and adults were suffering from impetigo contagiosa, two cases in the axilla, eleven on the face, neck, chest and abdomen, four cases generalised including scalp, one on the gluteal region and the rest of them on the face only. Except for two adults who were infected in the axilla and gluteal region, all these patients were in the age group of 3—16 years. The only treatment up to the time they came under my care had been calomel ointment.

In this large group of impetigo cases, there was thus an unusual opportunity to test the latest methods of treatment as recommended in the literature. There are three groups of drugs which are commonly used in the treatment of impetigo—the mercurials, the organic dyes and the sulphanilamide compounds. The success of local therapy depends upon two conditions (1) contact between the drug and the infectious agent, and (2) bactericidal potency of the drug employed. Contact can easily be established by removal of crusts before applying the drug, this has always been considered important in the success of the treatment. The choice of the drug naturally depends upon its effectiveness against the causative organisms. By the majority of dermatologists, impetigo is supposed to be caused

by streptococcus pyogenes as the primary agent and staphylococcus aureus as the secondary invader Carslow and Swenarton (1941) used sulphanilamide ointment with some success, although they employed it for only two days and then changed to other methods Their ointment was a complex one consisting of 5% sulphanilamide in glycerine, adeps lanae anhydrous, and paraffin molle flavum Mackenna (1941) has found sulphapyridine superior to sulphanilamide in its treatment A sulphathiazole 5% ointment in paraffin molle flavum was used with considerable success by A J Steigman (1942)

Sams and Capland (1940) used a 10% ointment of sulphathiazole in a cod liver oil base with equal success L H Winer and E A Strakosch (1942) found sulphathiazole effective in a water in oil emulsion, when the base was either cholesterinated petrolatum (aquaphor) or cod liver oil ointment

Authors who have used sulphathiazole as the chemical agent against impetigo have tried to stress the point that in some cases staphylococcus aureus may be the causative agent and in all cases it is present as a 'secondary invader' Sulphathiazole is the one drug of the sulphonamide family which is effective against both of these organisms These authors argue their case as follows "Whether or not staphylococcus aureus is present as a 'secondary invader' is important from the standpoint of epidemiology but is of no consequence from the point of view of selecting local therapeutic agents If the organism is present in abundance then it must be dealt with, even though it did not initiate the process" (Steigman, 1942)

In the case of these Polish children, a mercurial ointment (ung hydrarg ammon dil) was used for over a month which healed the lesions steadily but slowly, taking about 8—12 days to heal completely The importance of removing the crusts which forms over impetigo lesions to bring about contact between the bactericidal drug and the infectious agent has been mentioned above This is usually done by bathing in warm water, or better still, by warm olive oil compresses, or in bad cases by starch poultices Steigman (1942) used 'tinct sapo molles (BPC)' to remove the crusts In these children the crusts were removed by warm soap bath and a face flannel It was decided to use sulphanilamide powder against impetigo

instead of the mercurial ointment. The vehicle used for application of sulphanilamide as mentioned above has varied from the complex base used by Carslow and Swenarton (1941) to a simple base of soft paraffin. Here castor oil was selected as a base. It was with the idea that as olive oil is used to soften the crusts, without which their removal is painful and difficult, an oily base will keep the crusts soft and prevent them from drying, this was our experience in the present case. A thick suspension of sulphanilamide powder, 25 parts per 100 parts of castor oil was smeared on and rubbed into the lesions from which the scabs had been previously removed. The application was made twice a day. Definite improvement was noticed in 48 hours and the lesions disappeared in 4—8 days as compared with 8—12 days with the mercurial ointment. This reduction in the duration of treatment and striking improvement was noticed not only by the Polish nurses, who were in charge, but was commented on by the children themselves. Keeney et al (1941) and Steigmen (1942) have also noticed definite improvement in 48 hours though they used sulphathiazole. The latter also compared the clinical effects of 5% sulphathiazole ointment with those of ung. hydrag. ammon. dil. on the same patients and he also concluded that the former induces healing in approximately half the time taken by the latter. It can, therefore, be said definitely that sulphanilamide shortens the duration of treatment of impetigo and is superior to the mercurial ointments.

In conclusion, as far as the general state of health of these Polish refugees was concerned, it may be of interest to record that of the 42 children who were undernourished and complained of severe cough and who had their chests screened, only 6 had gross lesions in the lungs. One case was of pleurisy with effusion, three of infiltration in the upper lobes and two had broncho-pneumonic shadows. These children were screened again after a period of 28 days and as the lesions had not cleared up with treatment they were sent to a sanatorium.

Besides these, there were other minor illnesses amongst the children like diarrhoea, colds, tonsillitis and intestinal colic.

Summary

- (1) The health of some Polish refugee children during their stay in Bombay is reviewed

- (2) Sulphanilamide was used with success in impetigo contagiosa and the recent literature on its use and choice of the vehicles are discussed

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Case Reports

RAT BITE FEVER

A CASE WITH A LUMP IN A MUSCLE

By

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BOMBAY

In the August issue of the *Indian Physician*, R J Vakil and S M Shah described 'An Unusual Case of Rat Bite Fever with Multiple Lumps in the Muscles and Periosteum'. A similar case has come under my observation recently. Seeing the frequency of Rat Bite Fever in Bombay, the condition is rare and unfamiliar. It is not mentioned at all in the usual textbooks and as most of the practitioners are unfamiliar with it, there is no need for an apology for recording the following case.

R N N, a Hindu male aged 50, a sweetmeat maker, had a history of a rat bite a month before he sought medical advice. About two weeks after the rat bite on the dorsum of the left foot, he developed high temperature. The fever subsided, but the muscular and joint pains, and marked depression persisted. About two weeks later he developed acute bronchitis and low fever, for which he was sent to the P G Singhanee Hindu Hospital on the 5th September, 1942. He was found to be emaciated, and had a pale puffy appearance. He complained of depression, and pains in the joints and muscles. There was a healed scar on the dorsum of the left foot and there was slight swelling of the left foot. There were scattered râles and rhonchi on both sides. The cardiac apex beat was $3\frac{1}{2}$ inches from the mid-line, and the heart sounds were normal with regular rhythm. The spleen and liver were not palpable nor were there any enlarged lymphatic glands. The temperature was 99°F , the pulse rate 100 per minute and respiration 24 per minute. The urine, stools and sputum examination showed nothing abnormal. The routine blood count showed 4.3 million

red blood cells per cmm and 75% haemoglobin. The white blood cells were 18,000 per cmm with 85% polymorphs, 12% lymphocytes, 2% mononuclears, and 1% eosinophils. During the first week in the hospital he had a slight temperature ranging from 99°F to 101°F which settled down to normal on the 12th, after the use of Sulphapyridine for four days. The x-rays of the chest showed no lesion and the bronchitic signs gradually disappeared.

The blood examination for *spirillum minus* was negative and the clean mouse inoculation test was also negative after 15 days. The blood examination done again on the 16th September, 1942 showed a high leucocyte count of 17,000 per cmm. He had no rise of temperature since the 12th and as his blood examination was negative, I was reluctant to give arsenical injections, but in view of the persistent leucocytosis and the presence of muscular pains and mental depression, it was decided to give him intravenous Neosalvarsan. The first injection was given on the 23rd September, and the second injection on the 2nd October each of 0.3 gm. After each injection he felt better. As there was no rise of temperature at all he was given a discharge on the 14th October. During the night of the 14th, he developed an acute swelling of the left thigh. On the morning of the 15th when I saw him he had a large visible swelling in the middle of the left thigh, in front, which was about 4 x 3 inches in size, very tender to pressure, and of fairly hard consistency. It was freely movable in the muscle. The borders could be felt and rolled over quite well. It appeared like a hard fibroma. The skin over it was warm to feel, and a suspicion of an abscess was aroused. There were no other lumps anywhere else on the body. In the evening he developed a slight temperature upto 99.6°F. The blood count showed 20,000 leucocytes with 85% polymorphs. He was given 0.3 gm of Neosalvarsan intravenously. In about two days the swelling began to diminish in size and after about six days only a hard lump, about 1 x 1 inch in size could be felt in the thigh on deep palpation. A second injection of 0.3 gm Neosalvarsan was given on 23rd October. The blood count taken again on the 27th October showed 20,000 leucocytes with 67% polymorphs, 24% lymphocytes, 2% mononuclears and 7% eosinophils. No cause for this high leucocytosis could be

found on a careful clinical examination. The lump in the thigh had practically disappeared and one could feel only some induration of the muscle fibres on deep palpation. As there was no temperature, he was allowed to go home on the 30th October, in spite of the leucocytosis, with advice to return to hospital if he got fever or developed any muscular lumps.

This case shows many interesting features. He had a low irregular fever ranging from 99° to 101°F and never had the typical fever associated with a rat bite. This fever was controlled by sulphapyridine. He had a high leucocyte count throughout his stay in the hospital, 18,000 leucocytes per cmm on the 6th September, 17,000 on the 16th September and 20,000 on the 23rd October, in spite of four intravenous neosalvarsan injections. In spite of this high leucocytosis he did not have high fever.

In the absence of fever and any septic focus in the body it is difficult to explain this persistent high leucocyte count.

It is difficult to speculate on the nature of the lump which he developed on the thigh. It was a hard, tender gummatous lump which disappeared after intravenous injection of Neosalvarsan, and one feels that most probably it was connected in some way with the rat bite. The possibility of its being an abscess was considered, but in the absence of any fever and its rapid disappearance after Neosalvarsan, it was ruled out. In similar case it would be interesting to draw some serum out of it and inject it in a clean mouse to find out if it contains any *spirillum minus*. It will also be interesting to cut out a bit and to study its histological structure.

My thanks are due to Dr R. Row, M.D.D.Sc., Director of the P. G. S. H. Hospital and to Dr Kulkarni of the Pathology Department who did the mouse inoculation test for me.

Critical Notes and Abstracts

THERAPY OF RICKETS

E A Park, (I.A.M.A 1940 115, 370) discusses in detail the therapy of rickets. Rickets can be prevented and cured in two ways (1) by irradiation of the skin with ultra-violet rays and (2) by ingestion of Vitamin D. The skin is full of 7 dehydrocholesterol which is converted into Vitamin D by the action of ultra-violet rays impinging on the skin. Then it is absorbed into blood. There are as many as eleven forms of Vitamin D. Recent investigations have presented evidence of six different forms of Vitamin D in Cod Liver Oil. Out of these two are important, the first is activated ergosterol, the second, activated 7-dehydrocholesterol. All forms of Vitamin D are sterols closely related chemically. Vitamin D is soluble in oil and in most organic solvents, but not in water. Bile acids promote absorption of sterols, and so bile would be necessary for absorption of Vitamin D from the intestines. It is more stable than Vitamin B and C and it cannot be oxidized. No one knows how Vitamin D acts. It increases the absorption of calcium and phosphorus from the alimentary tract. It increases the metabolic rate. It seems probable that Vitamin D involves either directly or indirectly the parathyroid mechanism. *The unit of the Vitamin D* as adopted by the League of Nations Health Organization, is defined as "the Vitamin D activity of 1 mgm of the International Standard Solution of irradiated ergosterol found equal to 0.025 microgrammes of crystalline Vitamin D". The Steenbock unit is no longer used.

The available sources of Vitamin D

Cod Liver Oil contains at least 85 units per gram. However all Cod Liver oil marketed contain at least 100 units per gram. One teaspoonful of Cod Liver oil (4 grams) supplies at least, therefore, 400 units. Cod Liver oil is effective in rickets, infantile tetany and also ostomalacia. It is universally obtainable and safe and in addition contains Vitamin A about 600 units per gram. The great disadvantage is its lack of concentration, as it is not practicable to give more than 4 teaspoonfuls daily. The maximum dosage is limited to 1,400 units. Cod Liver oil is amply sufficient to prevent and cure rickets in almost all instances. Older children and adults will not take Cod Liver oil because of unpleasant taste. Infants, however, do not seem to mind the taste provided the oil is given regularly and early. When the infant refuses the Cod Liver oil, the fault usually lies with the mother or others who by words or action communicate their feelings. Many parents object Cod Liver

oil on the ground that it gives rise to digestive disturbances, especially in summer. The oil rarely does this and can be administered in hot weather without difficulty. However, some infants cannot take it and in very rare instances hypersensitiveness has been reported. If infants cannot take Cod Liver oil it is wiser to turn to other preparations.

Vioosterol in oil—Vioosterol in oil is ergosterol activated by ultra-violet irradiation dissolved in corn oil or some other bland oil. Vioosterol is a hundred times stronger than standard Cod Liver oil in Vitamin D content. It has no taste, consequently no difficulty is encountered in its administration. In the case of infants, it is best dropped directly into the mouth. It can, however, be dropped on orange juice in a tea spoon and in that way be floated into the mouth. It should not be added to feeding because a part may stick to the sides of the bottle and be lost. The only disadvantage that vioosterol has as compared with Cod Liver oil and other fish oils is that it does not supply Vitamin A. Vioosterol on account of its tastelessness and concentration is admirably suited for use of adults and older children. It is manufactured by (1) means of irradiation of ergosterol with short ultra-violet rays (the Steenbock Patent), (2) means of bombardment with low velocity electrons.

Vioosterol (Calciferol) in propylene glycol—Calciferol is activated crystalline ergosterol, in other words pure substance. Its special merit lies in the solvent employed. Propylene glycol is soluble in water hence vioosterol in propylene glycol can be mixed directly with milk.

Fish oils enriched with vioosterol or some other natural sources of Vitamin D—Halibut Liver oil is far richer than Cod Liver oil in Vitamin A but only four times more potent in Vitamin D. If vioosterol or some fish oil highly concentrated in Vitamin D is added to halibut oil it is possible to raise the Vitamin D concentration to that of vioosterol in oil and in that way obtain a product which is rich in both Vitamins D and A. The Vitamin A content of Halibut Liver oil is standardized at about 50,000 units per gram. The Vitamin D content is exactly the same as that of vioosterol.

Fish oils naturally concentrated in Vitamin D—The oil from different species of fish vary greatly in concentration of Vitamins A and D, some are rich in A, some in D, many in both. The order of fish richest in Vitamin D is Percomorphi. In the preparation of the oil for therapeutic use the manufacturers combine oils from various species in such a way that the final admixture has a concentration in Vitamin D equal to that of vioosterol in oil, namely 10,000 units per gram and a concentration of Vitamin A one hundred times that found in Cod Liver oil, namely 60,000 units per gram. These fish oils have the merit of providing Vitamin D and A in high concentration so that both can be ad-

ministered in doses measured in drops The taste is fishy, but the quantity required is small

Vitamin D Milk—Vitamin D can be placed in milk in three different ways *first* by ultra-violet irradiation, *second*, by feeding the cow with irradiated yeast, and *third* by adding a concentration of Vitamin D directly

The advantage of incorporating Vitamin D in milk is that it is taken automatically The disadvantage is that the amount of vitamin is determined by the milk requirement In other words the Vitamin D requirement may be insufficient though the milk is sufficient The requirement of Vitamin D seems to be dependent on age rather than on weight Three forms of Vitamin D milk may be regarded for practical purposes as having equal value Evidence suggests, however, that milk has too low a potency (135 units per quart) to be relied on for this purpose Four hundred units of Vitamin D per quart of milk may be regarded as the minimum concentration in that menstuum for the protection from rickets It is suggested in the case of fish oils and viosterol that from 800 to 1,000 units daily be regarded as lowest level that it is wise to employ for protection from rickets For practical purposes Vitamin D in viosterol may be regarded as being equal to Vitamin D of Cod Liver oil

Prevention of rickets—Since the period of greatest susceptibility to rickets is first months of life, it is important that full dosage of Vitamin D should be reached early, certainly by the end of the second month If Cod Liver oil be selected it should be started at the beginning of the third week or at the latest, the fourth week with a dose of one half teaspoon (175 units) This dose can be increased to 1 teaspoonful (350 units) after a few days In course of the next two weeks it should be raised to 2 teaspoonful (700 units) This dosage may be enlarged to 1,000 units (3 teaspoonfuls) or allowed to stand according to the need in the particular case It is certainly advisable to give 3 teaspoonful, if for any reason the infant seems to be particularly liable to rickets The dosage of 700 to 1,000 units should be continued throughout the first year As much as 700 units should be continued throughout the second year If real difficulties in administration of Cod Liver oil arise it is advisable to turn to one of the other preparations of Vitamin D A real danger in the use of Cod Liver is that it may cause Lipoid Pneumonia if it happens to run down the larynx into the lungs The use of concentrated fish oils, viosterol in oil is exactly the same as advised in the case of Cod Liver itself The administration should begin in the third or fourth week with a dose of 350 units reaching upto 700 units at the end of the sixth week It should be continued throughout the 2nd year Cod Liver oil or other anti-rachitic preparations should be continued throughout the summer provided it is well taken Premature infant is especially sus-

ceptible to rickets as well as to tetany and seem particularly liable to develop rickets. In these cases it is necessary to give Vitamin D in large doses upto 5,000 to 10,000 units or even more daily.

Cure of rickets—Although the doses of Vitamin D which are sufficient to prevent rickets in a given case can be relied on to cure the disease, the cure may take place slowly. It is better, therefore, to use sufficiently large doses to end the disease abruptly. Vitamin D milk is not sufficiently powerful in these cases. If Cod Liver oil is employed, the curative dose in the ordinary case of rickets is 1,000 units (3 teaspoons) daily. This dosage in the form of Cod Liver oil, the highly concentrated fish oils by viosterol preparations will bring advanced rickets under control within a period of three or four weeks in the great majority of cases. If the doses larger than 1,000 units are required it is best to use concentrated preparation of Vitamin D. In cases of premature infants it is sometimes necessary to give as much as from 10,000 to 20,000 units to bring the disease to a complete termination in a short time, and in some older children it is necessary to raise the dosage to 60,000 units daily or even in excess of that amount. When the rickets have been stopped the dose of vitamin can be reduced to protection levels.

The relationship of ultra-violet light to rickets—The rays of ultra-violet light which are active in the cure of rickets lie between 313 and 230 millimicrons. It was found that the radiation at 313 millimicrons exerted a slight anti-rachitic effect, the radiation at 302, 297, 280, 265, 253 millimicrons exerted a strong effect, those at 248 and 240 millimicrons, feeble effect and those at 237, 220 and 200 millimicrons no anti-rachitic effect whatever. Sunlight contains only one per cent of ultra-violet rays from 380 to 290 millimicrons. Ultra-violet rays shorter than 20 millimicrons are filtered by the atmosphere of the earth. Interposition of the atmosphere and the movement of the earth around the sun combine to cause a seasonal variation in both the quality and the quantity of the anti-rachitic radiations which reach the earth's surface. In summer ultra-violet potency of solar radiation is 10-14 times greater than that in winter. In polar region there is no ultra-violet rays. In equatorial zone ultra-violet rays are in abundance throughout the year. Diurnal variation in the anti-rachitic ultra-violet radiations also occur. During the early morning and late afternoon, when the altitude of the sun is low, sunlight does not possess any anti-rachitic activity. Naturally the period of the day when the sunlight is effective against rickets is longer during the summer than during the winter. The ultra-violet radiations of the sun may reach the body either directly or as a result of reflection. The reflected rays are known as sky shine, the direct rays as direct shine. In a room in a city ultra-violet sky shine will be effective only in 50 per cent if the windows are open. Glass windows and walls prevent reflected sky shine to come in the room.

Artificial sources of ultra-violet light —The artificial sources of ultra-violet light are quartz mercury-vapour lamp and the carbon-arc lamp, both are far richer than the sun's rays. The treatment with quartz mercury-vapour lamp may be conducted as follows: the lamp is placed at a distance of 2 or 3 feet from the body which of course is uncovered and the exposure of the front and back carried out alternately. The exposure is at first for one minute and is increased by one minute at each session until a total of 10 minutes is reached. The treatment is carried out every day or every other day. It must be continued for at least a month. For the prevention of rickets the irradiation may be carried out every other day and the duration of each session limited to two to three minutes. The treatment with carbon-arc lamp is conducted in a similar manner. The quartz mercury-vapour lamp is more apt to cause burns than the carbon-arc lamp. The burns produced by ultra-violet light are, however, exceedingly superficial (sun burn) and the inflammation disappears in a few days. When either lamp is used the eyes must be protected. Irradiation with ultra-violet lamps is especially valuable in conditions in which Vitamin D cannot be absorbed well from the intestine, e.g., obstruction of the bile duct. It also has been used to advantage in the protection and cure of premature babies. Ultra-violet rays can be used to supplement the administration of Vitamin D. Tanning is a useful sign that ultra-violet light is producing an anti-rachitic action.

The treatment of refractory rickets —Extremely large doses have to be administered in these cases. It may be necessary to administer up to 1,500,000 units daily. In some cases it has been necessary to raise the level of Vitamin D in blood 200 times the level considered as being normal. The cure of rickets experimentally produced in rats by means of citric acid-sodium citrate solution has been described. The mode of action of the citric acid-sodium citrate combination in rickets is not known. It should preferably be given in proportion of two parts molar citric acid to one part of molar sodium citrate. It has been found that deposition of calcium, under citric acid-sodium citrate treatment occurs at level which is considered below that necessary for deposition of lime salts in bone. This treatment can be used to supplement the Vitamin D treatment in rickets. Orange juice of five or six large oranges or 600 to 700 cc of orange juice taken daily increases the calcium, phosphorus retention and to a lesser extent the magnesium retention in the human being, orange juice can cure rickets probably by this calcium retention.

Signs of toxicity of Vitamin D —One need not fear that the dosage of Vitamin D will be toxic unless renal insufficiency exists or unless the dosage is extremely large. To adults, enormous doses of Vitamin D have been given over long periods without apparent injury. The symptoms of over dosage seem to be nausea, headache, diarrhoea, loss of appetite, frequent micturition and nocturia.

and lassitude. If the excessive Vitamin D therapy is continued undoubtedly the inorganic phosphorous as well as the calcium will become much elevated and metastatic calcification will occur.

J C P

THE TRANSMISSION OF KALA-AZAR

Hitherto the sandfly is suspected and there were very good epidemiological observations to believe that it is the transmitter of the infection of Kala-Azar fever. It was as early as 1924 Napier made observations that sandflies were present in quarters of Calcutta city where the Kala-Azar was endemic. At that time no infected flies were found but 40 per cent of the flies infected on Kala-azar patients developed a heavy flagellate infection in their midguts. Attempts to infect hamsters by bite of these sandflies failed except in two animals. From that time till to-day, from the circumstantial evidence, sandfly transmission was accepted as a working hypothesis. In 1939 Smith was again working to find out mechanism of transmission and the possibilities of sandfly control. Smith made some very important observations, namely (i) that after its primary blood-meal the sandfly could be kept alive for weeks by feeding on fruit juice, (ii) that if after a primary infected feed the sandfly was given another blood meal, the flagellate infection was likely to be knocked out or at least its activity was reduced, but that if the sandfly was fed on raisins, the leishmania infection increased until the whole pharynx of the fly was blocked with flagellates, and (iii) that the flies thus 'blocked' with heavy leishmania infection, although they attempted to feed when given an opportunity were unable to draw any blood, despite very violent efforts to do so. During these efforts it was certain that portions at least of the flagellate block became detached and entered the wound made by the proboscis. Swaminath conducted, repeated and extended Smith's experiments. Six human volunteers who lived in a hill district in Assam where Kala-Azar does not occur were selected, and infected flies were fed on them. At least three of these volunteers have contracted Kala-Azar. This is not sufficient proof, but taken in conjunction with all the rest of the observations that have been made on this disease, every scientist will agree that this experiment has removed the last objection to the already generally accepted conclusion that the usual method of the transmission of Kala-Azar is by the agency of the sandfly, *Phlebotomus Argentipes* in India and other allied species in other countries.

J C P

CADMIUM IN PULMONARY TUBERCULOSIS

Nizamuddin (Jr of Ind Medical Association, Vol XI, No 9, June 1942—265) reports the results of treatment of pulmonary tuberculosis by Cadmium in a series of 118 cases. He uses one per cent solution of Cadmium Sulphide in olive oil, 2 c.c. intramuscularly

once or twice a week. He considers it useful in chronic fibrotic and fibro-caseous type of lesions. The quantity of sputum became less, there was increase in weight and beneficial results were also seen in chronic bronchitis and pulmonary fibrosis. There is no contra-indication and it can be used in most advanced cases with or without complications. After giving ten injections usually an interval of one month was given before giving another course of injections. No serious unfavourable reactions have been noticed during the treatment. The results of treatment of the first series of 118 cases were

Clinically quiescent, and sputum negative	11
Much improved ambulant, afebrile with negative sputum	27
Improved, afebrile with positive sputum	50
Stationary, sputum positive	20
Worse	10

N J M

UREA AND ITS EFFECT OF TUBERCLE BACILLI

Professor Cummins, (BMJ, May 16, 1942), has shown that if suspensions of pure tubercle bacilli are mixed with various dilutions of urea, incubated at 37°C for 48 hours and then cultured on suitable media, urea in dilutions of half-saturation and one-fourth saturation completely kills off the tubercle bacilli from a thick emulsion in 48 hours. Wilson (1906) had also noticed the same phenomenon with coliform and other bacteria.

He observes that as urea either in the pure state or in saturated solution is harmless to the tissues and that it not only kills tubercle bacilli in very large numbers but also destroys septic secretions and ordinary saprophytes as well as pathogenic germs, it would appear very suitable as dressing for tuberculous ulcers and even perhaps for cavities close to the pleural surface, where adhesions have made these accessible or for small tuberculous empyemata. When crystalline urea is being used for the treatment of tuberculous ulcers, an oiled silk should be used between the urea and the dressings to protect its absorption by the dressings.

N J M

THE STATUS OF THE HEART IN PULMONARY TUBERCULOSIS

(Sweeney, J. A. Amer Heart Jour, 20 345 (1940))

This forms the subject of an illuminating paper by Sweeney who has analyzed the case records of as many as 1,585 patients of pulmonary tuberculosis for evidence of cardiovascular disease or derangement. The heart was found to be normal in most cases, in 3 to 5% of cases, tuberculosis involvement of either the pericardium, myocardium or endocardium was observed.

The characteristically "small," "pendulum heart" of pulmonary tuberculosis has been explained differently by different authors. According to some, the heart condition is primary and predisposes to the development of pulmonary tuberculosis by leading to a defective circulation within the lungs. On the other hand, others have regarded the smallness of the heart as being secondary to a tuberculosis toxæmia producing wasting, atonicity and degeneration of heart muscle tissue.

Tuberculous pericarditis undoubtedly represents the most frequent form of tuberculous involvement of the heart, being observed in about 3% of autopsies on tuberculous subjects. Three main forms of pericarditis are described: (1) Primary pericarditis, (2) Pericarditis associated with lung tuberculosis and (3) Pericarditis associated with extra pulmonary tuberculosis. Tuberculous pericarditis is easy to diagnose when there is active tuberculosis elsewhere in the body but in the absence of tuberculosis elsewhere (i.e., in the case of the so-called "chronic primary type" of Tuberculosis pericarditis) differential diagnosis from rheumatic pericarditis may present considerable difficulty. Features suggestive of the former diagnosis are: (1) Tendency to occur in the later decades of life, (2) A predilection for "coloured races", (3) The frequent absence of chest pain and disability, (4) Absence of joint pains, cardiac murmurs, and other rheumatic phenomena, (5) A hæmorrhagic effusion which may contain tubercle bacilli. Treatment comprises of paracentesis with air-replacement during the effusive stage and some form of operation as advocated by Beck during the "constrictive stage."

Tuberculous myocarditis, which is quite rare (only 222 cases having been reported until 1940) may be of three types: (1) The infiltrating type, caused by spread of the tuberculous process from the pericardium to the myocardium, (2) The nodular or miliary type, which is just a part of a generalized miliary tuberculosis, and (3) Interstitial tuberculous myocarditis, a rare form described by Gallavardin.

Tuberculous endocarditis is extremely rare, our knowledge of this entity is therefore quite meagre. According to Sweeney, there is no truth in the well-known statement that "mitral stenosis rarely occurs in cases of pulmonary tuberculosis." According to him mitral stenosis is observed in pulmonary tuberculosis with the same frequency as in other conditions.

A careful study of the blood pressure in cases of pulmonary tuberculosis at White Haven Sanatorium carried out over a period of ten years, has served to show the erroneous nature of the generally accepted idea that in pulmonary tuberculosis the blood pressure is below normal.

Coronary occlusion is seldom encountered in cases of pulmonary tuberculosis

R J V

A NEW DESIGNATION FOR THE R—T OR S—T JUNCTION OF THE ELECTROCARDIOGRAM

(Stern, N S Amer Heart Jour 20 355, 1940)

Recent electrocardiographic literature proves the importance of recognizing deviation ("elevation" or "depression") of the R—T or S—T segment at its origin (i.e., at its junction with the R wave or S wave). Such a deviation is usually referred to (even in the "nomenclature and criteria for Diagnosis of Diseases of the Heart") as "elevation (or depression) of S—T (or R—T) Segment at Origin". In order to avoid such lengthy and cumbersome phraseology, Stern has rightly appealed to the profession to accept his designation (viz., the letter J) for this junction between the R or S wave with the R—T or S—T segment. A high take-off of the S—T segment can then be simply referred to as a "High (or Elevated) J" and a low take-off as a "Low (or Depressed) J".

R J V

TREATMENT OF MALARIA IN SOLDIERS

The War Office has issued a pamphlet on the treatment of malaria in soldiers returning from service in malarious areas. The possibility of malaria should be remembered in cases of pyrexia without adequate cause, especially if associated with shivering, vomiting and subsequent sweating, where there has been recent service in a malarious area. Lack of facilities for making an exact diagnosis by microscopic examination of the blood should never cause delay in treatment.

The drugs recommended fall into two groups

- (1) Antisymptomatic and antipyretic for the acute attack
 - (2) Anti-infective and antirelapse after the acute attack
- The antisymptomatic drugs are quinine and mepacrine hydrochloride, the British equivalent of atabrine (German), (atabrine dihydrochloride N.N.R.) and quinacrine (French). The anti-infective drug recommended is pamaquin, the British equivalent of plasmoquine (German). Mepacrine and pamaquin should never be administered concurrently.

The standard army treatment of malaria is as follows

Days 1 and 2 Quinine bisulphate or hydrochloride, 10 grains (0.65 gm) in solution in 1 fluid ounce (30 cc) of water by mouth thrice in twenty-four hours

the rate suitable for the Indian masses By the way, why is this sulfathiazole not put on the market,—or at least supplied to the approved institutions?

There is another aspect of the question Are there no local cheap substitutes for Quinine? The Ayurvedic practitioners claim there are several Why can't a rapid survey of these be made by the Research Institutes and the Professors of Pharmacology and the public be made wise about it? In persons with sufficient immunity a number of drugs should control malaria, it is only in severe and malignant cases of malaria, and the primary infections of children and adults that potent anti-malarial remedies are needed

Bombay

A B C

Information

The Bombay Medical Union has requested us to announce that Members of the Medical Profession are invited to send a thesis or to deliver a lecture on any medical subject, preferably on any original or research work with reference to Indigenous Medicine on Western lines, for the award of the Sri Bhalchandra Krishna Memorial Fund Gold Medal Members of the Medical Profession include

All duly qualified Members of the Medical Profession holding degrees and diplomas from —

- (a) Indian Universities created by statute, and
- (b) Such other Universities and Corporate Bodies as the Managing Committee may from time to time determine subject to the approval of the General Body of the Union, and
- (c) Duly qualified Members of the Medical Profession holding Diploma of Membership of the College of Physicians and Surgeons of Bombay

The thesis or paper for lecture is to be submitted before the 30th March, 1943 to the Hon Secretaries, Bombay Medical Union, Blakesly Lodge, Bombay, for scrutinization by a Select Committee for making the award The thesis or the paper shall have to be read by the prizeman on the day of the award at the Meeting of the Profession to be held under the auspices of the Bombay Medical Union

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LIVERGEN

COMPOSITION

Indigenous drugs —

Andrographis Paniculata
Psychotria seed Fenugreek,
Hygrophila spinosa,
Oldenlandia corymbosa,
Carum Roxburghianum

B. P. Drugs —

Sodi phosph Sodi Benzons, Cascara
Sapra and bile salts etc

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Let us remember

INFECTION—HISTORICAL APPROACH

By

AMRUT V MODY,

M SC., (LOND)

BOMBAY

Historical approach to medicine makes us realise not only how developments in particular branch of theory markedly affects the growth of further ideas and researches, but also how a man can contribute to science even though he may not be highly academically qualified or possess well equipped laboratory and team of workers—the common excuse for the inactivity of the scientist and the doctor in India

This fact is well illustrated by following the development of the idea of infection and preventive medicine

Epidemics have broken out since ages past—various theories were also formulated besides magico-divine conceptions. Infection was compared to fermentation as in both occurrences there was rise of temperature, rapid spread, both could be propagated continuously without the diminution of the original focus, and both, as was thought till the time of Pasteur, could be ‘spontaneously generated’

The belief in spontaneous generation was popular since the time of Aristotle and earlier. It was believed that frogs originate from the mud of ponds and streams through sun’s rays. Even great Harvey, notwithstanding his bold sounding “*Ex-ovo Omnia*,” partly believed in this and Van Helmont had seen rats arise out of bran and old rags

Other great men like Buffon, Needham, Lamarck associated themselves with the belief in spontaneous generation. After Leeuwenhoek, the foremost microscopist of the 17th century, a number of minute animals, unicellular organisms, in water taken from rivers and lakes, partly in putrifying matter of various kinds, were observed and classified. They were called "Protozoa". Six years after his discovery of protozoa, i.e., in 1681, Leeuwenhoek discovered even more minute forms of life than these living atoms, namely "bacteria".

But this work actually revived and strengthened the hands of the believers in spontaneous generation. It was held that bacteria were the first stage of life originating from the inorganic material through natural agencies.

Italian Redi (1621-97) was first to make some experiments and suggested that the supposed products of life from non-living matter were always due to introduction of living germs from outside—if meat was covered with a thin piece of cloth, no worms arise in it inspite of putrefication. But he worked without the microscope and excited little enthusiasm in other workers.

Jan Swammerdam (1637-82) born in Amsterdam, associated himself with Redi. He went a step further and urged that so far from decaying matter producing minute living organisms, it is such living organisms that produce decay in organic matter.

It was left to Spallanzani of Bologna (1729-99) to prove after brilliant researches, that generation never takes place spontaneously. He boiled pieces of meat and vegetable matters and poured extracts into clean glass bottles with narrow necks which were soon sealed hermetically. It was found that the infusion remained clear without forming any scum on the surface, but when exposed to air it became turbid and showed presence of infusoria.

But opponents argued that heating the air in the sealed flasks had spoiled it for purpose of generation. Spontaneous generation in the presence of the unspoiled air seemed still to be a possibility. Pouchet (1800-72) brought out a large work "Heterogenie," his name for spontaneous generation. His elaborate details are now mere curiosities.

But as stated, earlier theories of fermentation and of spontaneous generation were linked up. Eminent chemists, Lavoisier and Berzelius studying the fermentation of alcohol discovered "diastase" and similar substances, "ferments" as they were called, and considered fermentation as a purely chemical process.

Chemists then believed that they had in their hands the substances that produce fermentation and similar processes. These chemical changes in the course of which albuminous compounds were formed as a by-product also gave a clear indication as to the direction in which the spontaneous generation of minute creatures might be looked for—fermentation was in fact a part of the process of spontaneous generation.

In 1836, the Frenchman, Charles Cagniard De Latour (1777-1859) suggested that the yeast really consists of minute organisms and it is their activity that causes the fermentation.

The above found a supporter in Schwann who in 1837 asserted that presence of yeast which consists essentially of a mass of plant-like beings is a condition of the alcoholic fermentation of sugar.

But it was left to Pasteur, a son of a country tanner, who studied under circumstances of privations and with numerous interruptions, to make crucial experiments which led to the downfall of the theory of spontaneous generation. His researches into isomerism led him to study the process of fermentation. He showed that fermentation was not due to chemical changes, but due to bacteria. He found a great variety of organisms associated with fermentation. Not all are of the type of yeasts—some are quite different in form. These are yet smaller and grow often in chains. Pasteur's investigations were summarised in his historic *Etudes sur le Vin* (Paris 1866).

Pasteur then took up the question of infection at the request of the French Government as silk industry was in decay. Long before him certain diseases of plants were well known to be due to and carried by gall-insects, aphides and other insects.

Agostino Bassi (1773-1856) of Lodi near Milan gave first demonstration in 1835 that a vegetable micro-organism could be a cause of infection. After series of investigations, Bassi

proved that a certain disease of silkworms was transmissible from moth to worm, and that the transmitting material was a minute fungus. In 1840 the Berlin Anatomist, Jacob Henle set forth in detail his theory that infectious disease is caused and conveyed by invisible forms of life.

Pasteur, after studying silkworm infections showed that there were two diseases and each associated with its own special organism. This was the most valuable hint which has opened out new departments of biology, initiated a new era in medicine and given a new view of the world of life.

Next disease studied was Anthrax. Koch, a country doctor, a man with poor education and little culture, now ranks with Pasteur as the founder of Bacteriology. He introduced the method of staining bacterial films with aniline dyes and of cultivating on solid media.

From 1870 to 1905, there followed that wonderful succession of discoveries which have distinguished for all the time the age in which we live, and which gave us the bacillus of leprosy (Hansen), the gonococcus, (Neisser), the typhoid bacillus (Eberth, Gaffky), the micrococci of suppuration (Ogsten), the bacilli of tuberculosis (Koch), of cholera (Koch), of diphtheria (Klebs Löffler), of tetanus (Nicolai), and of plague (Kitasato and Yersin), all between 1871 and 1894.

Thus with the complete downfall of the theory of spontaneous generation, and with the work of the bacteriologists, we have built up the modern conception of the bacillus as an agent, of the toxin as product of the bacillus, of the anti-toxin as the body's defence against the effects of the toxin. The contribution of Roux and Yersin, Mechnikov, Behring and Kitasato and others to the development of preventive medicine is fresh in the memory of all medical men.

So is also fresh in memory the development in the study of filterable viruses. Yet one thing is unknown. "How does an infectious disease originate in the first place?" Again scarlet fever, influenza, and other infectious diseases are very different in one year from what they were in another. Is it that the infective organism has changed or is it that the host has changed?

Thus it is still a long long way to speak of "the secret of disease."

Original Contributions

SHOCK AND ITS TREATMENT

By

B. B. YODH

M.B., M.R.C.P., D.T.M. & H.

BOMBAY

Shock can be conveniently defined as a clinical condition, associated with a reduction in the circulating volume of blood, coming on suddenly or insidiously and showing certain physical phenomena such as low blood-pressure, pallor, feeble pulse, cold extremities, etc

It is the usual practice to distinguish between primary and secondary shock but the fundamental basis is the same in both cases, that is, reduction in the circulating blood volume

Any kind of injury physical or mental may produce a sudden onset of fainting and unconsciousness associated with a low volume pulse and blanching of the skin and mucous membranes, the blood-pressure at this stage being often unrecordable. In the vast majority of cases, this is soon recovered from in a short time, the patient gains consciousness and the colour returns. This, so called, primary shock may have a nervous basis, the result of which is a sudden dilatation of the splanchnic blood-vessels along with a sudden reduction in the cardiac output. It is important to recognise this condition because it is common immediately after injuries and does not require any active treatment besides lowering the head of the patient for some time. The case of primary shock is distinguished from the more serious condition which appears later by the loss of consciousness which is constant, even if, it is present for a short time only. There is no loss of consciousness in shock that follows some hours after the injury.

After haemorrhage, internal or external, an injury with or without haemorrhage, burns and in some other conditions such as infections, poisoning and other toxæmias certain train of symptoms appear and which progress in many cases to a

fatal termination. These symptoms appear within a few hours after acute haemorrhages, severe injuries and burns and some toxæmias, but may appear after several days in infections. The onset of these symptoms is insidious and, therefore, if not looked for, the diagnosis may be missed and valuable time lost. Throughout the course the mind is clear and the patient may not feel ill nor complain of anything. Pallor is present in all cases but varies in degree, a cyanotic tinge may be seen over the nails, lips and lobules of the ears. The pulse is usually rapid and feeble, may be impalpable though in rare cases it may be normal and may mislead. The extremities are cold. The blood-pressure falls and goes on falling. The fall in blood-pressure appears to be the most constant guide in this syndrome and must be taken in every case and repeated at 15 minute intervals and charted. A continuous decline in the blood-pressure means shock and must be treated promptly. If the blood-pressure is 100 mm Hg or above, shock may be developing and a second measurement may prove it. If below 100 mm Hg and above 70 mm Hg shock is severe and if below 70 mm Hg it is very severe and recovery may not occur if treatment is delayed. The pressure may not be recordable in extreme cases. It will be noticed, therefore, that the recognition of shock depends upon very few physical signs and symptoms in its early curable stage and the only reliable guide is a steady fall in blood-pressure readings. In trying to understand the mechanism of shock in various cases it would be profitable to review the main conditions in which it appears and consider the factors likely to produce a reduction in circulating blood volume in these.

Haemorrhage External or Internal

Loss of blood from the circulation will obviously reduce the volume of circulating blood and is probably the most important factor. To maintain the circulation an intense vasoconstriction occurs which spares the vessels of the brain to a great extent and hence there appear pallor but no loss of consciousness. This pallor is seen even if the bleeding is not severe and as soon as blood volume is restored by administration of any fluid, not necessarily blood, it disappears. This vasoconstriction is maintained till the end in untreated cases.

and is responsible, if prolonged, for nutritional disturbances of capillary endothelium which may be permanent and which may so damage the capillary bed that treatment by administration of blood, serum, plasma or other fluids will be of no value as the fluid will filter out into the tissues. If haemorrhage is not severe, movement of the fluid from the tissues into the blood will be enough to restore the balance of the circulating volume of blood and the pallor will disappear without treatment.

Injuries

It is usual to have some bleeding in injuries and hence the loss of blood is an important factor here also. In addition to it, there is exudation of plasma in the traumatised area which further reduces the blood volume. If more plasma exudes in the tissues and if there is little haemorrhage, the red blood-cells are concentrated in the blood and circulation becomes more inefficient.

In burns, where shock is the most important cause of a fatal termination, plasma exudes into the tissues in enormous quantities producing inefficiency of the circulation both as a result of reduction in circulating blood volume and haemoconcentration.

Besides the loss of blood, as in haemorrhage and exudation of plasma into the tissues as in tissue injury and burns, other factors often aggravate the shock by further reducing the circulating blood volume. These factors are common to all the above conditions but the degree to which they operate varies considerably.

The state of hydration of the patient prior to the onset of the haemorrhage or injury is important. If loss of water has already occurred as a result of excessive physical exertion as in a millhand at work or a soldier on the march, the reduction of circulating volume of blood is increased many times over and the shock is increased far more rapidly. This factor is of very great importance in our country and must be taken into account in the treatment. It has been proved that dehydration alone can produce a state of shock by bringing about a reduction in circulating blood volume and haemoconcentration.

Pain is likely to be present in injuries and burns at least in the beginning. It has been thought that these painful stimuli, if continuously repeated, produce shock. It is also true that patients who are in a state of shock do not feel much pain and the pain may return if the shock is improved when the circulation is restored. Constant pain can, however, lead to widespread effects due to loss of sleep, constant movements, etc., and thus aggravate the loss of fluids and hence shock.

In outdoor work in tropical conditions and in warfare exposure to the weather—hot or cold—especially when they are extremes, leads to a further reduction in blood volume as a result of loss of fluids due to sweating, etc.

The diminished circulation has already produced a state of anoxia in the tissues and this is likely to be aggravated if there is an injury to the chest and difficulty in breathing. This will increase the cyanosis. Any additional infection which may supervene will aggravate the condition, as in severe infections the efficiency of the circulation is often impaired and a state resembling that of shock often appears in the terminal stages.

The various theories of shock so far put forward appear to be based on the study of the individual factors but probably many of the factors ultimately act in the same way, that is, by bringing about an increasing reduction in the circulating blood volume and when this becomes extreme an irreversible change occurs in the cells of the capillary endothelium, due to continued intense vaso-constriction and ischaemia. When this occurs, treatment cannot be of any avail and any fluids then administered will simply filter out into the tissues and not increase the circulating blood volume which is the purpose for which these fluids are administered.

Treatment

In the treatment of shock all these factors must be borne in mind. As has been said before, primary shock, that is, that which occurs dramatically and is associated with unconsciousness and pallor the only treatment is the recumbent position with the head low. Within a few minutes, colour and consciousness return and the pulse volume is restored. No elac-

borate treatment is necessary. If this has occurred in a patient who has had a severe haemorrhage or has been burnt or injured, watch for the other insidiously progressive condition of secondary shock which sets in from $\frac{1}{2}$ to 6 hours after the accident. That means keep a watch on the blood-pressure first and foremost, take it every 15 minutes and chart it, if it is progressively dropping, a condition of shock is being established whatever be the other signs and symptoms. Pulse is usually feeble and rapid but may not be so, pallor is usually present but varies considerably. Skin may be cold and clammy and signs of dehydration may be present but not necessarily so.

The sole aim and object of the treatment is to restore the circulating blood volume and that object is to be kept in mind throughout the treatment. The main things that require to be done are, therefore, stoppage of further blood loss as in haemorrhage, or plasma loss as in burns and tissue injuries. Counteract contributory factors such as dehydration by fluids, cold by moderate warmth and pain by a moderate dose of morphia if it has not been given before. Along with these and as soon as possible restore blood volume by administration of a suitable transfusion fluid.

As regards arrest of haemorrhage avoid tourniquets and apply pressure and bandage whenever possible. Plasma loss into traumatised tissues has to be avoided and if a tourniquet is applied it will have to be released every 15 minutes to prevent gangrene of the limb. Thus frequent release of the tourniquet will encourage plasma loss and hence will increase the condition of shock.

Application of a firm bandage (not tight) will help in preventing plasma loss in the traumatised limbs and should be considered in every case of injury or burns. Where a limb has to be amputated in any case, a tourniquet may be applied and never removed. The limb should be amputated above it. This will prevent shock in these cases.

Splinting or plastering limb, to immobilise it, also serves the purpose of limiting plasma loss. A single dose of morphia, gr $\frac{1}{4}$ in most cases, is permissible to relieve pain and anxiety. It should not have to be repeated. The time and quantity of

morphine should be noted on each case so as to avoid excessive morphinisation as this increases shock by producing anoxia by respiratory depression. The application of warmth should be done with discrimination. Too much heat will increase dehydration. Fluids by various routes are essential whenever there is evidence of dehydration. If the patient can drink, give water by mouth. The quantity to be given will have to be measured by gallons and not by ounces or pints. Even if the drink is refused, it must be forced. If there is no intra-abdominal injury, fluid should be forced by mouth even if there is vomiting. Add salt in the proportion of half a teaspoonful to each pint and sweeten the drink with sugar. As soon as hydration is established, urine secretion will increase and this should be charted. If water by mouth is not possible other routes should be used. The rectal, subcutaneous or intravenous routes may be used.

In order to give fluids rectally certain principles must be kept in mind. The rectum must be empty and in order to empty the rectum thoroughly, a bowel wash should be given. This wash should require at least 8 pints of fluid. The flatus that will collect in the rectum must be allowed an outlet so that the intra-rectal pressure does not increase and the sphincter is not forcibly opened. This is done by using a wide bore tube with several holes and not a catheter or single-holed enema nozzle. No clip should be used as the fluid is not given drop by drop but a column of fluid is maintained in the rectum from which absorption occurs. This column should not be higher than 4" and this is obtained by keeping the enema can containing the water at a height not exceeding 7" from the level of the anal orifice. If this is done 10 pints or more of fluid can be absorbed per rectum. It is usual for the rectum to absorb a pint in about 45 minutes. So that in 2 hours $2\frac{2}{3}$ pints are absorbed. Give rest to the rectum for an hour and the same can be repeated as required. The fluid used should be a mixture of equal parts of isotonic saline and isotonic glucose. Parenterally intravenously administered fluids are preferred to subcutaneously administered. To start with, give two pints of isotonic saline and then give alternate pints of isotonic saline and isotonic glucose or a mixture of both so that one pint contains half strength of each.

Salt used excessively may produce oedema and must be avoided

The rate of administration will depend on the state of dehydration and the presence of diarrhoea or vomiting. If blood-pressure is subnormal and dehydration extreme, give rapidly. The first pint may be given in ten minutes, subsequently slow down the rate to 80 drops a minute. It must be understood that this fluid will soon leave the blood and hydrate the tissues and hence the volume of circulating blood will not increase by this treatment and shock will not improve by fluids alone.

Oxygen is very essential if there is cyanosis. Pressure must be regulated and flow adjusted to 5 litres a minute.

While these things are being done, the main treatment, that is, restoration of the volume of circulating blood is obtained by transfusion. Transfusion fluids, having a higher osmotic tension, will remain in the blood vessels for a much longer period, i.e., about 6 to 8 hours and contribute enormously to the recovery of a patient in shock.

Transfusion must be carried out as soon as possible after shock is diagnosed. Delay is dangerous. A transfusion given late may be valueless as capillaries may have been damaged beyond repair due to severe ischaemia and the fluid simply passes through the blood vessels into the tissues and hence no increase in the circulating volume of blood occurs.

The selection of transfusion fluid is usually easy. If there is haemorrhage, blood is best. Blood can be stored for three weeks in a refrigerator and hence a supply may be available in well equipped institutions. If blood is not lost or only a little and the shock is presumably due to exudation of plasma into the tissues, serum or plasma are preferable. Both have a similar action and should be used promptly. A supply of these should be available in every institution. No grouping is necessary in pooled sera or plasma and a transfusion can be done immediately. Plasma may be life saving in shock due to burns.

If one remembers that the object of the transfusion is the rapid restoration of blood volume, the importance of the rate of administration and the quantity administered are easily

realised. In the beginning, in a case of shock, the transfusion must be rapid. First pint in 10 minutes, second pint in another twenty minutes and the third pint in further 30 minutes. This means that three pints are administered in about an hour. A quantitative restoration of blood volume is aimed at. There may be 40% to 50% of reduction of blood volume, i.e., of 1½ to 4 pints (1 pint is equal to 10% of blood volume of an average person). The patient improves remarkably quickly. Pallor disappears, pulse volume improves and pain, which may have been absent due to shock, now reappears. The amount to be transfused is determined by blood-pressure readings. A rise of 20 mm Hg after each pint is usual if haemorrhage is not continuing. When the blood-pressure reaches 100-110 mm Hg, reduce rate to 40 drops a minute (4 hours for one pint) especially in those cases where operation has to be done. Continue till operation is completed. In shock due to burns, the degree of haemoconcentration is an additional guide. Continue plasma transfusion till Hgb reaches 100% and then keep up a slow drip to counteract further plasma loss into the tissues.

(This article is largely based on the lectures delivered by Major General Marriot, R.A.M.C. at a recent Delhi conference on shock and resuscitation. Much original work has been done by him on the subject of wound shock resuscitation.)

THE ELECTROCARDIOGRAPHIC PICTURE OF PERICARDITIS WITH EFFUSION

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In spite of the massive knowledge that has accumulated within the last few decades on the subject of Electrocardiographic interpretation of heart-disease, one can truthfully say that our knowledge of electrocardiography with regard to diseased conditions of the pericardium still remains defective and controversial. It has rightly been remarked that "the diagnosis of acute pericarditis is more often missed than made". Such lack of interest in the case of the pericardial sac contrasts vividly with the voluminous literature that has accumulated on the subject of myocardial disease. Whatever little knowledge we possess on the subject of electrocardiography in diseases of the pericardium, we owe to a comparatively small group of workers (Schwab & Herrmann, Bellet & McMillan, Vander Veel & Norris to cite but a few) who have been persistently at it for the last thirteen years or so. This comparative lack of interest in the electrocardiographic pattern of pericarditis is attributable to three or four factors, viz, (1) The higher incidence and greater importance of myocardial diseases (2) The transient or evanescent nature of the electrocardiographic patterns in pericarditis. Such patterns, though characteristic are likely to be missed in the absence of serial electrocardiograms (3) The electrocardiographic alterations in pericarditis are, as a rule, not as striking or pathognomonic as in the case of myocardial diseases.

The importance of electrocardiography in the diagnosis of pericarditis has been stressed by Winternitz and Langendorf (1938). They observed that out of a series of ten fatal cases of purulent pericarditis, only two had been diagnosed correctly before death, in their opinion, as many as eight cases out of

these ten would have been correctly diagnosed and several lives certainly saved, if sufficient attention had been paid to the electrocardiographic tracings

According to some present-day writers on the subject, the electrocardiographic picture of pericarditis is sufficiently distinctive and characteristic to allow diagnosis. In the opinion of Billet & McMillan (1938), the electrocardiographic pattern of pericarditis "is distinctive enough to have diagnostic value"

An attempt will now be made to deal with the most important of the electrocardiographic changes or patterns that may arise in cases of pericarditis with effusion

Low Voltage It was in the year 1923, that Oppenheimer and Mann, for the first time, directed the attention of the medical profession to this important sign of pericarditis with effusion. That a marked reduction occurs in the size of the various deflections of the electrocardiogram in cases of pericarditis with effusion is now common knowledge

Oppenheimer and Mann (1923) when describing this feature of "low voltage" in seven of their cases of pericardial effusion published no electrocardiograms in support of their contention. In 1930, Scherf published the electrocardiographic tracings of a case of pericardial effusion exhibiting this feature of "low voltage", he demonstrated a striking increase in the amplitude of the various deflections after aspiration of fluid

Low voltage of electrocardiographic deflections constitutes one of the most striking of events in the electrocardiographic picture of pericardial effusion. It constitutes an early sign of effusion into the pericardial sac. The cause of "low voltage" in cases of pericardial effusion is explained by the majority of present-day cardiologists as follows (The Hypothesis of Oppenheimer and Mann). The presence of a good conductor like the mantle of fluid around the heart (in pericardial effusion), shunts or short-circuits most of the action currents with the result that only weak potentials are intercepted at the surface of the body by the electrodes, in other words, the feature of "low voltage" is attributable to a "short-circuiting" or damping of the electrical currents of the heart by a good conducting medium, viz., the pericardial effusion

The validity of this hypothesis has been proved by injecting normal saline into the pericardial sacs of animals and obtaining low voltage curves

Paracentesis or removal of a substantial amount of fluid from the pericardial sac in cases of effusion, frequently results in an increase in size of the various deflections. Though this phenomenon has been demonstrated convincingly from time to time by numerous authors, there are exceptions to the rule. For example, in a case of pericardial effusion reported by Schwab & Hermann (1935), the electrocardiogram taken soon after paracentesis showed a paradoxical and unexplained decrease in the size of the various deflections. In exceptional cases of even massive effusions into the pericardial sac, the amplitude of the QRS complex may curiously enough show little or no reduction in size. Such a finding is difficult to explain. According to Sherf & Boyd (1940) the following explanations are likely: (1) The mantle of fluid around the heart may be incomplete, (2) at some point or other, the heart may be adherent to the pericardial sac or to structures in the neighbourhood. Other possible factors, suggested by Schwab & Herrmann (1935) are myocardial oedema, pleural effusion, pulmonary engorgement and oedema of the subcutaneous tissues.

The Coronary Type of Electrocardiographic Pattern

Of the various abnormalities that may arise in the electrocardiogram in cases of pericardial effusion, deviations of the RS-T segment or sector from the iso-electric level and progressive alterations of the T wave are definitely the most striking and the most important. These electrocardiographic patterns of pericardial effusion bear such a close resemblance to those of myocardial infarction that a close study of the special characteristics of each type of electrocardiogram is essential for differential diagnosis. Progressive alterations in the electrocardiographic picture of pericardial effusion were demonstrated most clearly by Schwab & Herrmann (1935), making use of serial electrocardiography.

Historical In 1924, a case of pericardial effusion was reported by Gager with characteristic alterations of the S-T segments in Leads I and III and abnormalities of the Q wave, he demonstrated a disappearance of these signs immediately after

paracentesis, 500 c.c. of effusion being removed, a later follow-up of this case disclosed a progressive increase in the negativity of the T wave and an increasing depth of the Q wave

In 1925, Wood & White described a case of chronic nephritis with pericardial effusion where a marked upward deviation of the RS-T segment was noted in Leads I and II and a small upward deviation in Lead III. These alterations were attributed by Wood & White (1925) not to the pericardial effusion but to the toxic effects of the "uraemic poison" on the musculature of the heart

In 1929, Porte and Paidee described upwardly convex RS-T segments and "coronary type" of T wave inversions in the limb-leads of 3 cases of acute rheumatic pericarditis, they attributed these alterations to a co-existing inflammatory reaction within the myocardium. Scott, Feil and Katz, in the same year, reported the presence of RS-T deviations in 3 cases of pericardial disease. In a case of suspected rheumatic pericardial effusion, they described upward and transitory elevation of RS-T segments in all the limb leads. In another case of purulent pericarditis, they reported besides RS-T abnormalities, increase in the depth of the Q wave in leads II and III, these abnormalities were attributed to a state of anoxaemia of the heart-muscle, secondary to increase in hydrostatic pressure within the pericardial sac

Similar alterations or deviations of the RS-T segments and abnormalities of the T waves have been described in pericardial effusion by Agostoni and Papp (1927), Harvey and Scott, Purks and others

A Description of the Electrocardiographic Picture.

We owe our present-day description of the electrocardiographic picture of pericardial effusion to Billet and McMillan (1938), Vander Veer and Norris (1937) and Schwab and Herrmann (1935).

Schwab and Herrmann (1935) considered the electrocardiographic picture of pericardial effusion in 2 stages (1) The *early* or acute stage with elevation of RS-T segments and low voltage of the ventricular complexes and (2) the *later* stage, with progressive and retrogressive alterations of the T wave

Billet and McMillan (1938), on the other hand, consider the electrocardiographic pattern of pericarditis in 3 distinct stages, as in the case of myocardial infarction

The Acute Stage or "stage of RS-T Deviation" The electrocardiographic pattern of this stage, in the opinion of these authors, is so characteristic that it is "not encountered in association with any condition but acute pericarditis" This stage is characterized by an undirectional elevation of the RS-T segments in all the standard leads, though at times, the deviation may be restricted to Leads I and II only Though this description of "elevation of RS-T segments in all the limb leads" holds for the great majority of cases, it is well to remember that in the rare case of pericarditis with effusion, the RS-T segment in one lead, especially in Lead III may be actually depressed or below the iso-electric level Lack of appreciation of this anomaly has lead to erroneous interpretations in some cases The RS-T deviation is usually associated with a high "take-off" from the R deflection as in the case of coronary occlusion but at times the RS-T deviation arises in the absence of a high take-off, the deviation occurring after the R wave has returned to iso-electric level The T waves remain positive at this stage

The diagnostic criteria for this stage, laid down by Vander Veer and Norris (1937) are (a) lack of reciprocal displacement in Leads I and III, and (b) persistence of the R wave in Lead IV (new) even if the T wave in that lead becomes inverted

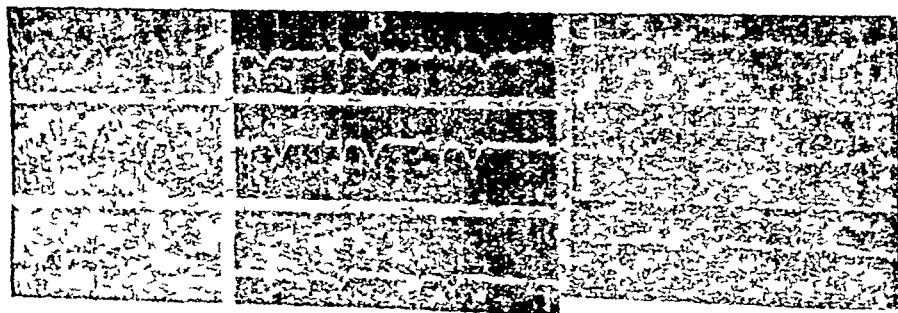


Figure A B C A, taken soon after the onset of pericarditis exhibits the typical RS-T type of pattern with upward deviation of RS-T in all the leads B taken in the T-stage or subacute stage shows inverted T waves of the Purdee type in the limb leads C taken in the chronic stage shows return of the entire tracing to normal. (From Belle and Mcmillan in Sircuda's Cardiovascular Disease)

With regard to the value of chest-leads in this stage, Schwab and Herrmann (1935) from an experience of only 2 cases, came to the conclusion that these leads furnish no additional information of diagnostic value. On the other hand, Billet and McMillan (1938) after making use of chest-leads in over twenty cases, found them very satisfactory, their use frequently associated with important information. The chest-lead may not only display the deviation of RS-T to better advantage but may disclose the deviation even when the limb-leads appear normal.

This type of pattern (stage of RS-T deviation) is said to arise in about one-half of all cases of acute pericarditis, it is said to be a transient phenomenon, seldom persisting in the limb-leads for more than 12 days, deviation of RS-T is said to persist in the chest-leads for a longer period of time than in the limb-leads (Billet and McMillan, 1938). In spite of the characteristic appearance exhibited by this electrocardiographic pattern, its importance is limited by certain factors, viz, (a) the phenomenon is transient or brief and therefore apt to be missed, (b) deviation of RS-T may be insignificant or limited to two leads only, (c) in some cases, RS-T deviation is altogether absent, (d) similar patterns may arise in other clinical states.

2 *The Subacute Stage* or the "stage of rapid T-wave changes". During this stage, there is a gradual return to iso-electric level of the deviated RS-T segments and the appearance of negative T waves. A characteristic resemblance to the "cove-plane" or Pardee T wave is frequently obvious at this stage. The inversion of T is either noticed in all the three standard leads or in Leads I and II only.

3 *The Chronic Stage*. During this stage, the inverted T waves show retrogressive changes. They may return to the normal upright position, may become flat or iso-electric or may remain inverted.

The above-mentioned "evolution" of the electrocardiogram is usually completed within a fairly short space of time, the electrocardiogram may have regained its normal contour within a few weeks. According to Roberts and Fulton (1938) once the cyclic progression of the electrocardiographic pattern is initiated in a case of pericarditis with effusion, it will continue inde-

finitely even if the tamponade is relieved. In certain types of pericarditis, e.g., uraemic, calcified or cicatricial, which are not accompanied by inflammatory foci in the subjacent myocardium, the electrocardiographic changes are "static" rather than "progressive" (Roberts and Fulton, 1938).

It is not possible merely on the basis of the electrocardiogram to gauge the severity or foresee the outlook in a given case of pericardial effusion. There is no evidence to substantiate the view that the degree of subjacent myocardial involvement or the size of the effusion is directly proportional to the degree of RS-T deviation or the degree of inversion or persistence of the T wave.

Billet and McMillan (1938) have commented on the aetiological relationships of the electrocardiographic alterations; they found inverted T waves with no significant deviation of RS-T segments as the usual change in cases of tuberculous pericarditis while most conspicuous feature was deviation of RS-T.

Causation of RS—T deviations and T wave changes.

Several theories have been put forward to explain the electrocardiographic pattern of pericarditis with effusion. The most important of these are

1 *The Theory of Cardiac Tamponade* (or the theory of Katz, Feil and Scott). This theory attributes the electrocardiographic alterations to modification of the coronary circulation caused by rise of intra-pericardial pressure.

Scott, Feil and Katz, in 1929, suggested as the cause of the electrocardiographic pattern, a state of coronary insufficiency induced by pressure of the pericardial effusion on the coronary arteries and coronary sinus. This was supported by experiments, in dogs, where similar curves were obtained after artificially forcing fluids into the pericardial sac. Schwab and Herrmann (1935) observed elevation of the RS-T segments in goats after the injection of fluids into the pericardial sac. They attribute the deviation to "ischaemia of the cardiac muscle", according to them, the intra-pericardial pressure "rises to the point of collapsing the auricles, thereby hindering venous return, lowering the systemic pressure and pulse pressure and thus interfering materially with the blood flow through the right and left

coronary arteries" It appears logical to assume that a rise of intra-pericardial pressure above the level of the intra-auricular pressure could easily impair the coronary circulation by embarrassing cardiac filling and by lowering the systemic pressure.

The following arguments have been put forward to contest the validity of this hypothesis.—

(a) According to Bellet and McMillan (1938), in the great majority of cases of pericarditis with effusion, the volume of fluid is not great enough to cause such striking alterations

(b) Vander Veer and Norris (1937) forward the argument that in man no relationship is demonstrable between the degree of the effusion and the degree of electrocardiographic alteration

(c) Even with massive effusions, the RS-T deviation may be absent, e.g., in the case of tuberculous pericarditis

(d) According to Bellet and McMillan, the very fact that RS-T deviations persist after adequate paracentesis is argument enough against the theory of tamponade

In the opinion of Schwab and Herrmann (1935), the upward deviation of RS-T in all the three leads is probably accounted for by the fact that both sides of the coronary circulation are involved in states of raised intra-pericardial pressure

2 *The Theory of Myocardial Injury or Sub-epicardial myocarditis* Narrow zones or foci or sub-epicardial muscle damage have been described for years in cases of acute pericarditis by prominent pathologists like Vaquez and Karsner. It is, however, to Fowler, Rathe and Smith (1923) that we must give the credit of first associating the electrocardiographic alterations of pericarditis with these sub-epicardial lesions within the musculature of the heart. They obtained in dogs, curves similar to those of coronary occlusion, by merely opening the sac of the pericardium, they showed that these electrocardiographic changes were invariably associated with superficial myocardial lesions or processes, e.g., inflammatory foci, patches of fragmentation and vacuolation of muscle fibres. Vander Veer and Norris (1937) demonstrated the existence of "sub-epicardial myocarditis," microscopically, in cases of pericardial

effusion with RS-T deviations This theory has gained further support from the work of Bellet and McMillan (1938), Burchell (1939), Scherf and Boyd (1940) and others

According to Scherf and Boyd (1940), sufficient evidence has accumulated to prove that irritation, chemical or mechanical, of even minute areas of the epicardium or the subjacent myocardium, is sufficient to induce profound alterations in the electrocardiogram

3 *The Theory of "disturbed" neuro-myocardial balance*
This theory can be said to be still in the making Recent experiments on the nervous innervation of animal hearts, have served to show that disturbances in "neuro-myocardial balance" may induce striking alterations in electrocardiographic tracings

Alterations of the T wave, encountered in the later phases of the electrocardiographic pattern of pericardial effusion, have been attributed by Schwab, Herrmann (1935) and others to "process of organization and repair" within the epicardium and the subjacent layers of the myocardium According to these observers, the T wave changes are qualitatively independent of the aetiological factor or factors concerned, e g, rheumatism, tuberculosis

Differential Diagnosis

That a similarity exists between the electrocardiographic pattern of pericardial effusion and that of myocardial infarction (especially of the anterior wall type), there is no doubt whatsoever This similarity is not surprising in view of the fact that from the physiological disturbance point of view, the lesion in the two cases is closely similar, according to Roberts and Fulton (1938), the common dominator in the two cases is "myocardial injury," in the one case deep and circumscribed, in the other superficial and generalized

In order to facilitate the problem of differential diagnosis between coronary occlusion and pericardial effusion, an evaluation of the essential differences between the electrocardiographic patterns in the two cases, is essential Features of diagnostic import are —(1) The evolution of the electrocardiogram is more rapid in the case of pericardial effusion and the whole picture may be completed with a return to normal within the

space of a few weeks (2) with regard to the RS-T segment, the deviation is upward in Leads I and III, the reciprocal relationship of these two leads (such as is witnessed in cases of coronary thrombosis) being practically, never observed in cases of pericardial effusion (3) Schondorf's sign Schondorf (1936) stressed the importance of observing the contour of the RS-T segment In coronary thrombosis, the RS-T segment is convex upwards while in pericardial effusion it is concave upwards, in other words, it is "dome-like" in coronary thrombosis and "trough-like" in effusion (4) Q waves are, as a rule, normal in size and shape in cases of pericardial effusion, though exception do occur On the other hand, in coronary occlusion, conspicuous alterations in the depth or contour of the Q wave are most frequent (5) Abnormalities of the initial ventricular deflections are much more frequently observed in cases of coronary occlusion (6) Though the inverted waves of pericardial effusion do bear a certain resemblance to the Pardee T wave of coronary disease, they rarely attain the great amplitude of the latter The very tall T waves of coronary disease are not a feature of pericardial effusion

According to Bellet and McMillan (1938), the electrocardiographic picture of pericardial effusion is strikingly similar to that of "cardiac infarction involving the anterior and posterior walls of the left ventricle" (the Wood-Wolferth-Bellet syndrome) Since the RS-T segment is uniformly elevated in the three leads of the electrocardiogram in both these conditions, the distinction may prove very difficult The following features should suggest the possibility of the condition being coronary infarction rather than effusion, viz, (1) the presence of a prominent Q wave in Lead II or III, (2) abnormalities in the configuration of the QRS complex (3) If the deviation of RS-T in Lead III is slight or insignificant (4) If the RS-T deviation in Lead II corresponds (approximately) to the algebraic sum of the deviations in Leads I and III (Bellet and McMillan, 1938)

Miscellaneous Changes

Other abnormalities have also been described in the electrocardiogram of pericardial effusion, from time to time (1) *Heart-block* In 1924, Gager reported a case of pericardial effusion with auriculo-ventricular block which disappeared

completely after paracentesis Agostoni and Papp, in 1927, reported two cases of pericardial effusion of rheumatic type, where auriculo-ventricular and bundle-branch conduction defects were combined (2) In a case of pericardial effusion described by Schwab and Herrmann (1935), the *P wave* was "sharply peaked" and of high voltage in Leads II and III, a striking alteration in the size and configuration of this wave was noted after paracentesis (3) Prominent or abnormal *Q waves* have occasionally been described in the case of pericardial effusion Such abnormalities have been reported by Gager (1924), Scott, Feil and Katz (1929), Agostoni and Papp (1927) and by Schwab and Herrmann (1935) (4) Slurring or notching of the QRS complex has been noted by several observers This was noted fairly frequently in my series of cases (5) A characteristic type of *T wave* has been observed by Schwab and Herrmann (1935) and described in detail by Bellet and McMillan (1938) in cases of pericarditis "Taking origin at or slightly above the iso-electric line the gradual or more or less normal upstroke of the *T wave* is followed by a sharp, breakline downward dip, which inverts the terminal portion of the *T wave*" (Bellet and McMillan)

For the sake of convenience in classification, Noth and Barnes (1940) considered the electrocardiographic pictures in cases of pericardial effusion, under the following heads (1) Pathognomonic, (2) strongly suggestive, (3) suggestive and (4) not suggestive Out of their series of 53 tracings, 3 were considered pathognomonic, 22 as strongly suggestive, 11 as suggestive and 17 as not suggestive

Duration of the Electrical Systole or the Q-T Interval

According to Tung (1941) this affords an objective criterion which may aid in differentiating "cardiac dilatation with congestive failure" from massive pericardial effusion, a differentiation often difficult or impossible in clinical practice

In the electrocardiogram of congestive heart failure, a prolongation of electrical systole at the expense of diastole has been demonstrated by Beck (1937) Tung found in a series of cases of pericardial effusion that the electrical systole or Q-T interval was shorter than the predicted normal value (calculated according to Adam's formulas) by about 14%

He found that instead of a relative prolongation of the Q-T interval as occurs in cases congestive heart failure, cases of massive effusion showed Q-T intervals either normal or shorter than normal

The value of constant $K = \sqrt{\frac{Q-T}{R}}$ in cases of pericardial effusion varied from 0.344 to 0.434 with a mean value of 0.393, while similar values in normal subjects as determined by Shipley and Hallahan were, a range of 0.337 to 0.433 with a mean of 0.397 for males and a range of 0.380 to 0.456 with a mean of 0.415 for females. According to Tung, the fact that the Q-T duration is normal in cases of massive pericardial effusion may have a theoretical as well as practical value in differentiating cardiac dilatation from pericardial effusion

Present Study

Analysis of Material For the purpose of this study we collected a small series of 28 cases of pericarditis with effusion from the records of the K E M Hospital, Bombay. The cases were aetiologically of varied types.

Electrocardiographic Findings

1. *Voltage or Amplitude of Deflections* In this series of cases, the amplitude of the P wave ranged from -1.0 to 2.2 mm with a mean value of 0.67 mm (normal values of P for Indian subjects, range -2.0 to 3.2 mm with average of 1.0 mm).

The amplitude of QRS ranged from 1.3 to 4.9 mm with an average of 3.2 mm (normal range 0.9 to 22.0 mm with average of 9.15 mm).

The amplitude of T ranged from -1.4 to 2.6 mm in this series, with a mean value of 0.15 mm (normal range = -4.2 to 10.1, average = 2.1 mm).

From the above data, it is obvious that a diminution in the amplitude of the deflections is almost a constant feature of pericardial effusion, also, the auricular deflection or P is not spared by the low voltage, though the effect on P is not as marked as it is on the ventricular deflections of the cardiogram.

2 *Duration of Waves* This was calculated in the case of the P wave, the QRS complex and the T wave. The P wave duration ranged from 0.04 to 0.14 sec with an average of 0.10 sec (normal range 0.03 to 0.11 sec, average=0.073 sec). The T wave duration ranged from 0.04 to 0.20 sec, with an average of 0.14 sec (normal range 0.10 to 0.29, average=0.17 sec). From the above, it is apparent that pericardial effusion has little or no influence on the duration of the electrocardiographic deflections.

3 *The Duration of P-R* (P-R interval) varied from 0.10 sec to 0.24 sec with an average of 0.165 for the 28 cases, (normal range 0.07 to 0.21 sec, mean=0.147 sec.) In other words, there is a tendency for the P-R interval to show a slight increase in cases of pericardial effusion. Whether such an alteration is caused by the "active rheumatic process" or whether it is the direct result of the effusion, one cannot say.

4 A tendency to slurring or notching (pathological) of the QRS complex was noted in as many as 8 out of the 28 cases, i.e., 29% of the cases. In 6 out of the 28 cases, (i.e., 21.4%) a curious type of M-shaped QRS complex was noted. In 5, this was observed in Lead III and once in Lead I.

5 *RS-T Deviation* An RS-T deviation over 1 mm was observed in 12 of the 28 cases (43%). In 3 cases, the upward deviation was confined to Leads I and II only, in the rest, it was observed in all the limb-leads.

6 In as many as 5 records, the Q wave was prominent in Lead III or in Leads II and III.

7 In one case, there was associated auricular fibrillation while in another there was complete heart block.

Summary

- 1 The importance of electrocardiography in the diagnosis of pericardial effusions has been stressed. Familiarity with the electrocardiographic picture of pericarditis is essential if confusion with other diseases is to be avoided.
- 2 Characteristic electrocardiographic patterns are described and their pathogenesis discussed.

- 3 The electrocardiographic findings in a series of cases of pericardial effusion from the files of the K E M Hospital are presented and discussed

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THE RADIOLOGICAL DIAGNOSIS OF PERICARDIAL EFFUSION

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The diagnosis of pericardial effusion, in clinical practice, may be attended with considerable difficulty. The differential diagnosis of pericardial effusion from simple dilatation of the heart may tax the diagnostic acumen of the clinician to the utmost. Though a massive literature has accumulated on the subject of pericardial effusion and innumerable physical signs have been described from time to time as aids to diagnosis, our knowledge regarding the radiological diagnosis of this condition remains vague and contradictory. Roentgenological examination is of value in cases of pericardial effusion, not only for the purposes of diagnosis but also for the proper follow-up and treatment of the case. When diagnosis is in doubt, the final decision may rest with the radiologist. A perusal of the literature on the radiological diagnosis of pericardial effusion leaves us unsatisfied, clearly defined statements are lacking, our knowledge of the subject is disseminated and controversial. For the guidance of the busy diagnostician, the present paper is intended to present a formulated summary of our present day knowledge on the subject of Radiology in the diagnosis of pericardial effusion.

As early as 1903, Dr Francis Williams²² described the radiological appearances of the chest in cases of pericardial effusion. In the case of large effusions, he described an increase in size of the cardiac silhouette, a "rounded" contour of the heart and obliteration of pulsation along the left cardiac border. In the case of small effusions he made observations on the influence of posture on the silhouette of the heart.

The minimal amount of effusion that can be detected radiologically is about 250 cc according to Hugo Roesler (1937)¹⁶ and from 300 to 400 cc according to Kerley (1939)⁷. Accumu-

lations of fluid smaller than these are not detectable by clinical or roentgenological methods; they are usually diagnosed in the autopsy room.

In the radiological diagnosis of Pericardial effusion or the exudative form of pericarditis, the following signs are worthy of note.—

1 *Increase in size of the cardiac silhouette* This depends not only on the amount of pericardial effusion but also on the size of the heart. With effusions smaller in amount than 300 c c, no enlargement of the cardiac silhouette is apparent. With massive effusions, on the other hand, the cardiac shadow may occupy a very large part of the thoracic cage.

2 *Change in shape of the cardiac silhouette* The shape of the cardiac silhouette varies enormously in different cases, depending not only on the size of effusion but also on the type of the heart, the shape of the thorax, the degree of associated ventricular hypertrophy, etc. The cardiac silhouette in cases of pericardial effusion has been variously described in the literature as "roughly triangular," "spherical," "pyramidal" and "pear-shaped." It has been compared to a "tobacco-pouch" (Kohler, 1931),⁸ "a leather water-bottle with sagging sides," "a round bottle with a short neck" (Freedman, 1939)³ and "a flask with a short neck." According to Freedman,³ the cardiac configuration of pericardial effusion is by no means pathognomonic, it may be encountered in cases of cardiac decompensation.

3 *Holmes' Sign⁶ or The influence of posture on the shape of the cardiac silhouette.* In 1897, Shattuck¹⁷ remarked on the influence of posture on the shape of the cardiac dullness (percussional) in cases of pericardial effusion. In 1920, Holmes⁶ gave a detailed description of the alterations in cardiac contour induced by postural changes, in cases of pericardial effusion, he noted these phenomena in all of his cases of effusion. In the recumbent position (prone or supine), the cardiac dullness rises high in the chest with an increase of width at the base, in the standing or erect position, the increase in width of the cardiac silhouette is just above the level of the diaphragm (Holmes, 1920).⁶ This phenomenon, described independently by Shattuck (1897)¹⁷ and by Holmes (1920),⁶ has since been

confirmed by numerous writers on the subject. In the recumbant position, the heart shadow tends to be "globular" or "spherical" in shape while in the upright posture, it becomes "pyriform," "pear-shaped" or like a "water-bottle." In Freedman's opinion,³ this sign is of the utmost value in the differential diagnosis of pericardial effusion from enlargements of the heart. The one great drawback of Holmes' Sign is that it cannot be made use of in orthopnoeic and in moribund cases.

4 *Obliteration of the normal "hollows" or "angles" of the heart.* The normal "hollows" or "angles" of the heart, shadow, which serve to demarcate the various chambers of the heart, become obliterated or flattened out in cases of pericardial effusion. There is no actual bulging of the cardiac silhouette at these points, unless encapsulation of fluid occurs, such an encapsulation on the right border of the heart has been referred to in the literature as "Kienbock's Inflammatory Diverticulum." Holmes (1920)⁶ has described an "absence of the normal outline of the various chambers" of the heart, in cases of effusion. Kohler (1931)⁸ describes a "loss of sharpness of contour of the heart shadow" with "filling out of the complementary spaces of the heart," while Roesler (1937)¹⁵ describes a "Straightening of the waist of the heart."

5 *Rotch's Sign¹⁰ or Obliteration of the cardio-hepatic angle.* In 1897, T M Rotch¹⁰ described an increase of cardiac dullness to the right in the 5th and 6th inter-costal spaces with "obliteration of the cardio-hepatic angle" in cases of pericardial effusion. For some years, medical opinion was in accord with Rotch's views, the idea prevalent being that in pericardial effusion, the right cardio-hepatic or pericardiophrenic angle (which is normally "acute") becomes "obtuse." Recent work by radiologists and others has shown the erroneous nature of this hypothesis. In 1917, Morris and Bader,¹² by artificially producing pericardial effusions in cadavers, showed that injection of the pericardial sac with as much as 1,500 cc of ascitic fluid was incapable of obliterating the cardio-hepatic angle. Holmes (1920)⁶ found the cardio-hepatic angle in his cases of pericardial effusion, sometimes "acute," sometimes "obtuse" and sometimes "obliterated"; he found similar alterations in cases of cardiac dilatation. In the opinion of this author,⁶ the cardio-hepatic angle is more

to become "obliterated" if the examination of the patient is carried out in the standing position. The prevalent opinion at the present time in radiological circles is that the cardio-hepatic angle in cases of pericardial effusion, far from becoming "obtuse" becomes "sharply acute", the clinical demonstration of a positive Rotch's Sign in these cases is accounted for by "the small amount of resonant lung-tissue" contained within the narrowed cardio-hepatic angle.

6. *Lack of visualization of cardiac borders within the pericardial shadow.* It was maintained by certain radiologists of the old school that the heart shadow can be visualized within the pericardial shadow as a "denser nucleus" in cases of pericardial effusion. The experimental work of Holmes (1920)⁶ has served to explode this old theory, he found that the radiographic demonstration of the heart shadow within the shadow of artificially induced pericardial effusions is practically if not quite impossible.

7. *Disproportionate increase of the Transverse Diameter of the heart or Vaquez' Sign.*^{20, 21} According to Vaquez and Bordet (1920),²⁰ an unusual or disproportionate increase in the size of the transverse or horizontal diameter of the heart (in relation to the longitudinal diameter) is characteristic of pericardial effusions, though a similar disproportion may also arise in the case of cardiac enlargements, it is never so pronounced.

8. *A rise in the upper border of the cardiac shadow.* The upper border of the cardiac silhouette tends to rise towards the episternal or suprasternal notch in cases of pericardial effusion (Shirley Smith, 1937)¹⁸

9. *Dietlen's Sign or Shortening of the vascular pedicle.* The importance of this sign in the diagnosis of pericardial effusions, has repeatedly been affirmed by Vaquez,²¹ who describes it as Dietlen's Sign. There is an obvious shortening of the vascular pedicle in these cases. Kerley (1939)⁷ describes in cases of this sort, "a very small aorta resting on top of a very large heart", this is particularly so with the patient lying down.

10. *Shirley Smith's Sign*¹⁸ *or Widening of the vascular pedicle.* According to Shirley Smith (1937),¹⁸ there is a definite

increase in the width of the vascular pedicle at the level of the second inter-space in cases of pericardial effusion, the width attained in such cases may be twice normal

11 *Williams' Sign*²² In pericarditis with effusion, the shadow of the inner or medial part of the diaphragm on the left side becomes obscured or obliterated, this sign is difficult to elicit

12 *Destot's Sign* In cases of effusion within the pericardial sac, there is a downward prominence or "bulging" of the pericardial shadow on the left side, to a level well below that of the diaphragm, this "bulge" may be visualised as an opacity within the "gas-bubble" of the stomach

13. *A diminution in the pulsation of cardiac borders.* In the great majority of cases of pericardial effusion, there is a definite diminution or even absence of pulsation of the cardiac borders. Though this sign may serve to distinguish pericardial effusions from cardiac hypertrophy where pulsations of the cardiac borders are unduly vigorous, it is of no value in the differential diagnosis of effusion from cardiac dilatation. According to Holmes (1920),⁶ diminution or absence of pulsation occurs with the same frequency in cardiac dilatation as in cases of pericardial effusion

14 *Change in the character of cardiac pulsations.* There is a definite change or alteration in the character of the pulsations of the cardiac borders, in cases of pericardial effusion, the altered pulsation has been described as "Worm-like," "wave-like" or "diffuse and undulating"

15 *Loss of pulsation of the inferior border of the cardiac silhouette* It is said that loss of pulsation when it affects the cardiac borders, starts first in the inferior border of the heart, which can be seen through the "gas-bubble" of the stomach, during fluoroscopy. This sign has been described in association with even small effusions of fluid in the pericardial sac. The character and amplitude of pulsation of the inferior border of the cardiac silhouette can be seen to advantage by artificially inflating the stomach; this can be achieved with the use of an effervescing mixture

16. *According to Holmes (1920),⁶ the normally distinct and asynchronous pulsations of the auricle and ventricle become indistinguishable in cases of pericardial effusion*

17. *Berner's Sign*.¹ According to Berner (1937),¹ the co-existence of a normally pulsating aorta with an abnormally or feebly pulsating left cardiac border should suggest the possibility of pericardial effusion

18. *Roesler's Sign*¹⁵ or *Distension of the posterior inferior recess of the pericardium*. In the opinion of Hugo Roesler (1937),¹⁵ an early sign of pericardial effusion is a "filling up" or "distension" of the posterior inferior recess or sinus of the pericardial sac, this can be displayed to advantage in the lateral or oblique positions. Instead of being straight or slightly concave as in normal cases, the contour of this recess, in cases of pericardial effusion, becomes convex, this is most evident at the level of the inferior vena cava. Roesler's sign may be positive even with small-sized effusions, it is difficult to interpret when there is a co-existing pleural effusion. According to Pendergrass (1927),¹³ the "bulging of the posterior inferior reflection of the pericardium to the diaphragm" can be seen to best advantage during sustained inspiration, with the patient standing in the lateral position. Frederic Tice¹⁹ directs attention, in cases of pericardial effusion, to "alteration in shape of the angle formed by the posterior border of the heart, the diaphragm and the spine"

19. *Fleischner's Sign*. Fleischner maintains that even a small pericardial effusion can be diagnosed by noting "an abnormally convex bulging of the posterior surface of the heart" in the lateral position

20. Daily or rapid, fluctuations in the size or alterations in shape of the cardiac silhouette should suggest the possibility of effusion (Freedman, 1939)³

21. According to Kerley,⁷ a feature worthy of note in cases of effusion is the frequent absence of pulmonary hyperaemia or congestion, in spite of a massive heart shadow

22. *Berner's Kymographic Sign*.¹ Kymographic recording of the pulsatory amplitudes of the aortic knob and the left ventricle, in cases of effusion, reveals vigorous pulsation of the aortic knob in association with a poor pulsation of the left ventricle, when the effusion clears the pulsatory amplitudes become equal again

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SCABIES

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Etiology

The disease is caused by the *acarus* or *sarcoptes scabiei hominis*. The female after impregnation burrows through the horny layer of the skin leaving in her wake ova. She is a tiny white speck just visible to the naked eye. She has eight legs, conical in shape. The front ones being provided with suckers and the hind ones with bristles. Her structure permits her to move forward only so that eventually she dies in the grave that she has dug. The male is about half the size of the female and lives on the surface of the skin. After impregnation of the female, he dies.

The ova hatch out every three to six days and the escaping larva, burrows its way to the skin surface to reach adult-hood. The disease is contagious and it is usual to find several or all the members of a household affected.

Symptoms

The characteristic of this disease is itching which is usually worse at night. The clinical picture varies very much in people of dirty habits and others of cleanly ones. In some people it is extremely difficult to diagnose, the burrows appearing very sparsely.

Distribution

The typical distribution is — the fingers, the axillary folds, around the umbilicus, the inner surface of the thighs, over half the buttocks. In some people the whole body is affected with a second crop of impetigo. In addition to the face, the neck, On the face, the character of the disease may be more frequent in women.

her suckling infant It is only these infants who get the disease on the face Children also have the palms and the soles affected Contact must be fairly prolonged to acquire the disease, e g, from a sexual partner, or sleeping in the same bed with an affected person or wearing infected clothes

Diagnosis

This is easy in a straightforward case, but in some people the rash is so misleading, so sparse, that much difficulty might be experienced in detecting the disease The secondary impetiginisation might be so severe as to confuse the picture The itching is, however, usually a prominent feature and especially so at night time

Treatment

The aim of treatment is to destroy the burrow and the acarus It should be fairly prolonged as the larvae hatch out at intervals of 3 to 6 days, and short—24 hour—treatments unless given to hospitalised patients usually fail to cure The classical treatment of scabies is with sulphur ointment The dose for an adult is 10% of sulphur precipitate in one ounce of vaseline Balsam of Peru may be added in a strength of 5% with advantage

As important as the medicament is the method of its application The following instructions should be given On the first night a hot bath with soap, which should be well rubbed into the affected parts A brush may be used with advantage as it will assist in opening up burrows Too vigorous treatment may give rise to a severe dermatitis and should be avoided After the bath the ointment should be well massaged into the skin on the affected sites chiefly, and on the rest of the body from the neck to the soles of the feet The patient then is instructed to sleep with the ointment on Next morning a similar rub is given and the ointment is kept on all day In the evening another rub and the ointment is kept on all night On the following day again a morning and an evening rub On the fourth day in the morning the patient should have a bath and all clothes worn by him, all bed, linen, etc, should be thoroughly boiled, or disinfected

After this treatment some people develop a dermatitis due to the application This is easily relieved by a soothing

application such as Calamine liniment. Recurrence is due to improper treatment or re-infection, e.g., a child bringing the disease back into the family from an infected playmate. Treatment should not be repeated for at least 10 days. Many other preparations have been employed for the treatment of this disease. In the Hospital St. Louis in Paris, the patient is given a one day treatment where a preliminary bath and scrub is followed by the application of sulphur ointment. The patient's clothes are meanwhile disinfected and he is allowed to leave the premises at the end of the day. Benzyl-Benzoate incorporated in a preparation has also recently been advocated, as a one day treatment. These treatments unless under strict supervision give rise to recurrence.

Benzyl-Benzoate is very much used in Denmark and was introduced by Kissmeyer in 1937. The advantages are the shortness of treatment, the absence of a greasy application in contact with the skin—as in sulphur treatment,—the patient being able to go about his business in comparative comfort. A lotion is made up consisting of equal parts of Benzyl-Benzoate, soft soap, and methylated spirits. The patient is instructed to have a hot bath with soap, a brush may be used with advantage as it assists in opening up burrows. The lotion is then well rubbed in, particular attention being given to the affected areas. After a few minutes a second rub is given. The medicine should be allowed to dry on the body, any excess may be removed with a towel. The patient then wears his clothes and goes about his work for 24 hours. He then has a bath in hot water and gets into clean clothes, the discarded ones being sent to the dhobi or may be boiled at home. Recurrence of the infection is rare and a second treatment may be given after as short an interval as four days. When contrasted with the treatment by sulphur ointment, Benzyl-Benzoate has much to commend it.

War conditions all over Europe have caused a tremendous increase in the incidence of this disease. New and improved methods of treatment are said to be in use but unfortunately they are very hush-hush, we will have to wait till after the war, to confront the acarus in this country with a new and improved technique of destruction.

Case Reports

ACUTE PERICARDIAL EFFUSION A REPORT OF FIVE CASES

By
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(With 8 x-ray figures on plate)

Case 1 DV, male, aged 22, complained (4-2-1941) of pain in the chest, pain in joints and irregular fever of some two months duration. The past history was negative. On examination the area of cardiac dullness was found to be increased and there was some congestion of the veins in the neck, the liver was palpable and tender. There was some dullness at the left base and the air entry was poor. A to and fro murmur was heard at the base of the heart. The clinical examination suggested pericarditis with effusion. The blood-pressure was 140-80 mm Hg. The blood count showed 3.3 million red blood cells per c.mm., 64% hemoglobin, and 9,750 white blood cells per c.mm. with 70% polymorphs and 20% lymphocytes. He had a temperature ranging between 97°F and 100°F. The blood count done on the 10th, showed 15,650 white blood cells per c.mm. His x-ray (Figs 1 and 2) examination showed a huge cardiac shadow which suggested pericardial effusion. A needle was inserted in the pericardium on the 10th, and 20 cc of haemorrhagic fluid was removed, it showed a large number of red blood cells, and polymorphs. No organisms were detected and the culture as well as the mouse and the guinea pig inoculations were negative. On the 17th, 200 cc of haemorrhagic fluid was removed, and he was put on M & B 693, one tablet four times a day. In three days the temperature became normal and remained normal till his discharge from the hospital on the 12th March, 1941.

Case 2 D.P.N., aged 22, male, came (15-4-1941) as an out-patient complaining of breathlessness for 7 days, and pain in the epigastrium for one month. The history was that he had fever for a few days, two months before he came to the hospital, which had subsided. The pain in the epigastrium had appeared a month ago which was getting worse, and for the last 7 days he was getting breathless on the slightest exertion, and had even difficulty in talking. The past history was negative, there was no history of tuberculosis in the family.

On examination he showed a slight cyanosis and engorgement of the veins in the neck, the liver was palpable and tender. The area of cardiac dullness was considerably increased and there was dullness in the second left inter-costal space at the base, the

heart sounds were inside the area of cardiac dullness and were distant and feeble. There was no pericardial friction. On the back there was dullness at the left base, and bronchial breath sounds. The pulse rate was 100 per min and showed extra-systoles. Pericardial effusion was suspected and he was admitted in the ward. His blood count showed 3,000,000 red blood cells per cmm, 57% haemoglobin, and 4,350 white blood cells per cmm. The x-ray examination (Fig 2 and 3) showed no definite pulsation of the heart, and an enlarged cardiac shadow. The electro-cardiogram taken on 18th April, shows inversion of T waves in lead I and II. He developed fever in the ward, and a paracentesis was performed on 18th April, 200 cc of brown haemorrhagic fluid was removed, it showed a large number of red blood cells, degenerated leucocytes, and a few endothelial cells. No organism was present and the culture was negative. His temperature persisted, and he was tapped a second time on 29th April, 150 cc fluid was removed. He left hospital against medical advice after two days. He continued to attend the out-patient department, and remained in a good condition till about a year, when he had to be admitted twice in the wards with signs of adherent pericardium and a double murmur at the base. He was discharged each time after some weeks' rest and treatment and finally returned again to the hospital on the 17th November 1942, in an advanced stage of congestive cardiac failure and died on the 23rd November 1942.

Case 3 C A, a male Hindu aged 30, sought advice on 9-5-1941 for continuous fever and cough of ten days' duration. On examination he showed dyspnoea, slight cyanosis, and some congestion of the veins in the neck. The pulse rate was 124 per min, feeble and of low tension. The temperature was 101°F. The apex beat could neither be seen nor felt. The area of cardiac dullness was considerably increased, the left border being a little beyond the anterior axillary line, the right border was 2" from the mid-sternal line, and there was a submanubrial dullness in the second inter-costal space. At the left base there were dullness and bronchial breath sounds. The liver was palpable, three fingers' breadth from the costal margin and was tender, the spleen was not palpable. The blood count showed 5 million red blood cells per cmm, 75% haemoglobin, and white blood cells 5,500 per cmm with 68% polymorphs and 28% lymphocytes. The sedimentation rate was 45 mm in one hour. The x-rays (Figs 5 and 6) showed a considerable increase in the cardiac shadow. A diagnosis of pericardial effusion was made and on 10-5-41 paracentesis was performed and 400 cc of clear serous fluid was aspirated from the pericardial sac. The examination of the fluid did not show any organisms, the cultural examination for tubercle bacilli and other organisms was also negative. The fluid began to refill again and he was tapped again on the 17th, as he showed signs of cardiac and respiratory embarrassment,—1,100 cc of fluid was removed and 400 cc of air was left in the pericardium. Again

the fluid began to refill rapidly and the area of cardiac dullness extended beyond the mid-axillary line and on 22-5-41, 1,500 cc of pericardial fluid was aspirated and 340 cc of air was left in the pericardial. He was put on short-wave diathermy, he showed some improvement, the fluid did not reappear, the temperature settled down; but on 9th June, 1941, he developed a painful swelling of the right thigh and leg suggestive of femoral thrombosis. The pulse became irregular and feeble, and he developed signs of congestive cardiac failure. He was put on digitalis, ammonium chloride and salyrgan injections, but showed no improvement. His condition became gradually worse, and he died on 30-6-1941. No post-mortem examination was available.

Case 4 R.B., a Mohamedan male, aged 35, came to the hospital on 6-6-1941, for fever for four weeks and pain in the right upper quadrant of the abdomen for a fortnight. The fever was associated with rigors, the pain was dull, aching in character and more or less continuous. There was rigidity of the right upper rectus. The liver was enlarged and tender, the spleen was not palpable. The white blood cells were only 5,650 per cmm. The examination of the heart and the chest showed no abnormality on the day of admission. As the x-ray machine was out of order it was not possible to screen him or take a plate. A tentative diagnosis of amoebic hepatitis was made, and he was put on a course of emetine injections. The fever which ranged between 98°F and 104°F settled down after six injections of emetine and he was making a satisfactory progress, but on the 16th June, he began to show general weakness. The apex beat was not visible or palpable and there was an increase in the area of cardiac dullness. The pulse was feeble and rapid. On the 18th, he was screened when the cardiac shadow appeared to be greatly enlarged, and the cardiac pulsations were not visible, the diaphragm moved well, and the dome on the right side was not elevated. The diagnosis of pericardial effusion was made and on the 21-6-41, 90 cc of fluid was aspirated. It was turbid and reddish brown in appearance and showed 420 cells per cmm most of which were polymorphs. The blood count showed only 2,250 white blood cells per cmm. He developed an irregular temperature and his general condition got worse and worse. He was tapped again on the 9th July, and 300 cc of purulent effusion was removed. He did not show any improvement and his condition steadily deteriorated. On the 21st, 600 cc of pus was removed from the pericardial sac and he died on the 29th July 1941. Surgical interference was considered, but the patient had refused. No post-mortem examination was available.

Case 5 B.R., a Hindu male aged 30, came to the out-patient department on 18-7-1941 for pain in the right hypochondrium and breathlessness for 15 days. The patient had low fever at night for about 10 to 12 days about a month ago. About a fortnight ago, he started getting severe pain near the 8th rib on the right costal mar-

gin The pain used to radiate to the xiphisternum, the pain was very severe and he had to lie down Six days ago he applied some leeches over the right hypochondrium but had no relief The patient when seen was very dyspnoeic, cyanosed and restless He was acutely ill and appeared to be in agony The jugulars of both sides were greatly engorged The cardiac impulse was neither visible nor palpable They area of cardiac dullness was considerably increased, the left border being $5\frac{1}{2}$ " and the right border being 4" from the midline The heart sounds were very feeble, almost inaudible There was dullness at the left base, and coarse rales were heard at both bases The air entry was deficient, the blood pressure was 100 mm of mercury systolic and 70 mm of mercury diastolic The pulse rate was 112 per minute, the blood count showed leucocytosis of 17,550 per c.mm of which 78% were polymorphs and 18% lymphocytes The x-ray examination (Figs 7 and 8) showed a marked increase in cardiac shadow A diagnosis of pericardial effusion was made and a paracentesis was performed and 15 oz (450 cc) of fluid were removed on the 18th July, i.e., the day of admission The pericardial fluid was turbid, and yellowish in colour and the predominant cell was the polymorph Three days later, as the condition did not show much improvement, another paracentesis was performed and 750 cc of fluid were removed, the fluid that came out today was turbid and reddish brown, the typical anchovy sauce appearance of liver abscess There were no amoeba or cysts in the fluid It was suspected that the liver abscess had ruptured in the pericardium and the patient was put on the injections of emetine He did not show any improvement and as the area of cardiac dullness increased, another aspiration was done on the 26th and 750 cc of purulent fluid were removed, even after this he showed no improvement and the fluid kept on refilling and on the 3rd August, 1,000 cc of fluid was aspirated Another aspiration was performed on the 9th August and 750 cc were removed Nine days later, the clinical examination suggested pleural effusion as the result of repeated punctures and 1,800 cc of purulent fluid were removed from the pleural cavity A week later he was aspirated again and 650 cc were removed The fluid examination throughout did not show any organisms except bacillus pyocyaneus which was considered to be a contamination, throughout this period he had no temperature On 31st August he was transferred to the surgical side for pericardiotomy At the operation it was found that there was a communication between the pericardium and the liver The patient did not rally after the operation, his condition gradually got worse and he died on 8-9-1941 A partial post-mortem was performed which showed that a tropical abscess of the liver had ruptured into the pericardium

Comment

Cases of acute pericarditis with effusion are rare, still one meets them rather not infrequently at times, as shown by the



Fig 1 Radiograph of case 1 D V, an enlarged cardiac shadow



Fig 2 Radiograph of case 2 D P after removal of fluid and (Pneumopericardium)



Fig 3 Radiograph of case 3, R B to 28 6-41 showing an enlarged shadow

N. J MC



Fig 1 Radiograph of Case 1 (Mrs K) taken showing a greatly increased area of card



Fig. 111 Radiograph of case 5 R B taken on 29 6-41
after removal of fluid and introduction
of air

RICARDITIS WITH EFFUSION



Fig 2 Radiograph of the same patient taken a month later, on
22 11-41, showing a practically normal shadow

above five cases which were seen by me in the course of five months, from 14th February 1941 to 18th July 1941. The diagnosis of pericardial effusion is not difficult if the condition is kept in mind and a careful clinical examination is made. In all the above five cases the diagnosis was first made clinically and then only confirmed by x-ray examination and by the needle.

The first three cases appear to be tubercular, though no tubercular bacilli were seen. All three had haemorrhagic acute effusions. Case one kept on attending the out-patient department, for a year but has not returned since. Case two developed adherent pericardium and later congestive cardiac failure which ended fatally in November 1942—i.e., he lived for nineteen months after the effusion. The last two cases were of amoebic hepatic abscess which had ruptured into the pericardium. This is not a very frequent complication of amoebic abscess, but should always be kept in mind in unusual cases.

There should be no hesitation in doing a pericardial puncture if an effusion is suspected. Apart from its utility for diagnosis, it is often necessary for treatment. By relieving the pressure it may prevent an oncoming congestive cardiac failure. Often patients ask for it, so great is the subjective relief after removal of the fluid from the pericardial sac. One can say little about its effect on the future development of the disease especially as regards the development of adhesions. Case two above, who was tapped twice with much subjective relief developed a severe type of adherent pericarditis. Putting in air after removal of the fluid may help in some cases, but not in all, as air or oxygen is absorbed very rapidly. Once the adhesions have formed, it is difficult to introduce any air, even under high pressure. Apart from the removal of fluid and introduction of air or oxygen, there is no special treatment for acute pericarditis. Short wave therapy or deep x-ray therapy has been suggested in suitable cases. For purulent pericarditis, sulphanilamide group of drugs may be tried with advantage, where patient's condition permits, pericardiectomy should be advised if simple aspiration fails. This may be required also in serous or haemorrhagic effusions, where repeated punctures fail to relieve the patient.

PERICARDITIS WITH EFFUSION

A REPORT OF TWO CASES

By

N J MODI,

M B, M R C P (LOND)

(With 2 X Ray Plates of Case I)

Case 1 Mrs KD, aged twenty, housewife, was admitted under my care in Sir Harkishondas Hospital on 22-10-41 for cough with expectoration, and dyspnoea on exertion for the last four months, and oedema all over the body for the last fifteen days. History of miscarriage one year back otherwise nothing of importance in the past or family history.

On examination the patient was markedly pale, slight oedema was present all over the body, but no free fluid was detected in the abdomen. Nails and conjunctivae were pale, tongue pale and glossy, teeth dirty. Posterior cervical glands were palpable. Liver was tender and enlarged two fingers breadth below the costal cartilage, and the spleen was also palpable.

Scattered rales and rhonchi were found in both the lungs. Examination of the cardio-vascular system showed the apex beat on palpation in the left sixth inter-costal space, five inches from the mid-sternal line, on percussion the left border of the heart was six and a half inches from the mid-sternal line in the left sixth inter-costal space, showing the dullness extending well beyond the apex beat. Clinically there was also evidence of the right and the upper border extending beyond normal limits. On auscultation the first and second sounds were heard, a soft systolic murmur was heard at the mitral area, which was conducted into axilla, and also a systolic murmur at the pulmonary and aortic area was heard. The pulse was 120 per minute, regular and slightly collapsing in nature. The blood-pressure was 140 mm of mercury systolic and 50 mm of mercury diastolic, on admission. The clinical findings suggested pericarditis with effusion, which was confirmed on x-ray (Fig 1), examination.

The laboratory investigations showed a low blood count of 1 12 million red blood cells per cmm and 20% haemoglobin (Shali's Haemometer), and total white cells 4,680 per c mm on 23rd October, 1941. Urine showed no abnormality except a faint trace of albumin. Blood urea was 55.5 mgms per 100 cc of blood on the 25th of October, 1941. No growth was detected in blood culture done on 29th October, 1941.

About 30 cc of pericardial fluid was aspirated by me on the 29th October, the pathologist reported a few pus cells and no definite organisms found, culture of the pericardial fluid was sterile.

She was given sodium salicylate grs XX with same amount of sodium bicarbonate three times a day, one Digoxin tablet B D, 4 cc of Liver intramuscularly every day, 20 grs of Blaud's mass B D, and intravenous glucose with Vitamin C daily. After ten days glucose with Vitamin C and digoxin were omitted. The patient was also getting diuretin powder grs X B D.

The progress of the patient is well illustrated by the following blood counts —

23rd Oct 41	R. B C	1 12	Million per c mm	20%	Haemoglobin
29th Oct 41	R B C.	1 51	"	25%	"
5th Nov 41	R B C.	1 79	"	31%	"
12th Nov 41	R B C	2 01	"	40%	"
19th Nov 41	R B C	2 71	"	50%	"
26th Nov 41	R B C	3 25	"	65%	"
3rd Dec 41	R B. C.	3 62	"	70%	"

The patient was discharged on the 11th December, 1941 cured of her anaemia and no evidence of any pericarditis (Fig 2).

Case 2 G V, aged 40, sex male, was admitted on 25th September, 1941 under my care in Goculdas Tejpal Hospital, for breathlessness on exertion, pain in the chest of three months' duration and pain in the right hypochondriac region, which was increasing. In the beginning the breathlessness was only on exertion, but for the last fifteen days, the patient was dyspnoeic even at rest and had cough at night.

On examination the patient was well-built and nourished, there was clubbing of nails, no evidence of anaemia, the supra-trochlear and posterior cervical glands were enlarged

Examination of cardio-vascular system showed no precordial bulging or visible pulsation on inspection. Apex beat on palpation was in the left sixth inter-costal space, anterior axillary line. The upper border of the heart on percussion was at the third rib, right border one inch outside and the left border extended upto the angle of scapula in the sixth inter-costal space. On auscultation a soft systolic and diastolic murmur were heard all over the precordium, but best heard in the left second and third inter-costal spaces. The pulse was ninety-six per minute, regular and water-hammer type. Blood pressure was 110 mm of mercury systolic and 60 mm of mercury diastolic, there was no difference in both the arms.

Moist sounds were heard at both the bases in the lungs, but no impaired note. The clinical findings suggested a combination of aortic lesion and pericarditis with effusion. The presence of pericarditis was confirmed by x-ray on the 26th of September.

The blood examination showed, total red blood cells 4.1 million per cmm, Haemoglobin 78%, total white blood cells 7,300 per cmm, urine showed nothing abnormal. The blood for Wasserman reaction was positive.

The patient was treated with sodium salicylate grs XX, three times a day, with intravenous glucose and Vitamin C.

The blood sedimentation rate was five mms at the end of one hour. Gallop rhythm was noticed on the 7th October, and patient complained of pain in the right hypochondriac region and epigastrium after food with flatulence.

On 17th October, 60 cc of pericardial fluid was aspirated by me. The laboratory report was,—cells, mostly lymphocytes, occasional polymorphs, organisms,—large number of organisms of various types including spore bearing (extraneous?). Acid and alcohol fast bacilli present.

On account of the report, patient was given 10 cc ten per cent. calcium gluconate intravenously daily for some days,

also anti-syphilitic treatment was started, a course of Bismostab 1 cc, twice a week was given intramuscularly:

On the 25th of October, pulsation in the precordial area was seen, apex beat was in the sixth left inter-costal space, four inches from the lateral sternal line Diastolic thrill and murmur were found at the base, gallop rhythm also continued.

Patient was slightly better for a few days, he was aspirated again, but this time no acid or alcohol, fast bacilli or any other organisms were found, and it was concluded that in the last report the finding of organisms was probably a result of contamination This was later proved on post-mortem examination

The patient gradually became worse and developed oedema all over the body and died on 18th February, 1942

The post-mortem report was as follows —

External examination —A body of a male aged forty, well built and well nourished Oedema all over the face, abdominal wall and legs Scar on glans penis Marked clubbing of nails and also of great toe nails On opening the body about 200 c c of bile stained free fluid was found in the peritoneal cavity Free fluid was also found in the pleural cavities On the left side the visceral and perital pleura were adherent to each other and also with the pericardium at the apex Heart was enlarged, the pericarditis was found, but the two layers of the pericardium were quite separate except at the apex At the base of the heart, *bulging from the left ventricle was a big aneurysmal sac about the size of a tennis ball* A probe could be passed into the sac from the left ventricle The aorta showed characteristic syphilitic patches Liver and spleen were enlarged and congested Both the lungs showed congestion at the bases Kidneys, intestines and the bladder were normal Microscopic examination of sections taken from the heart showed characteristic specific endarteritis

These two cases are reported, as they are examples of rarer causes of pericarditis with effusion, the first due to anaemia and the second due to syphilitic involvement of the heart

(I wish to thank Dr F N E Moss, M.D (Lond.) Superintendent G T Hospital for his permission to report case two.)

Critical Notes and Abstracts

INTESTINAL CHANGES IN MONKEYS FED ON POOR RICE DIETS

As a result of experiments carried out in Coonoor during the years 1918-21 McCarrison reached the conclusion that "the health of the gastro-intestinal tract is dependent on an adequate provision of accessory food factors" and he noted that "experiments with animals have led us to expect that acute intestinal disorders will be among the commonest of the consequences of deficient and ill-balanced food" McCarrison's experiments were carried with diets which were grossly deficient in vitamins and essential food factors, and produced deficiency states rapidly in animals which succumbed in 2 to 3 months Dr M V Radhakrishna Rao, (Ind Jou. Med Res, 30, 2nd April, 1942) carried out experiments on monkeys fed on poor rice diets for a long time resembling those consumed by human beings in India The production of any specific type of deficiency disease was not aimed at The most important observation made during the investigation—an observation not anticipated at the outset—was the tendency of the deficiently fed monkeys to develop chronic diarrhoea, accompanied by specific changes in the small intestine, which have been described in detail in this paper Young monkeys (*macacus sinicus*) from 4 to 7 lbs in weight captured in jungles were used The animals at the outset appeared healthy and were not suffering from diarrhoea, dysentery, or other gastro-intestinal disorders Blood examination showed no evidence of previous protozoal infection They were kept in the place for about a month before being put on the experimental diets

At the beginning of the experiment, the animals were divided into two groups, A and B The sex ratio and the average and individual initial weights in the groups being very nearly the same Animals in group A were fed on a fairly well-balanced lacto-vegetarian diet (diet A), based on whole wheat, milk, vegetables, pulses and fruits, resembling that consumed by certain races in North India Group B was fed on a diet which is known in the Laboratories as the 'cheap Madrasi diet' or the 'Poor South Indian Diet' (diet B) and resembles that consumed by poor rice-eaters in India as ascertained from results of numerous diet surveys It consisted mainly of milled rice, a small quantity of various kinds of pulses, and vegetables and condiments 'Protective foods' such as milk, milk products, meat eggs, etc, which are occasionally taken in small

quantities or not at all by the poorer classes were not included in basic ration. Diet B was given in cooked state. The monkeys on diet A consumed all the fruits and vegetables and practically all the milk. A variable proportion usually about one-third, of the whole wheat chapatti, was often left unconsumed. The cooked rice and soup of diet B were mixed well, made into a bolus and offered *ad lib* to the animals. Diet A was superior to diet B, in respect of nearly all the important food factors. The latter was deficient in Vitamin A and C, Vitamin of B group and calcium. The animals were kept in separate cages under hygienic conditions and were housed in airy rooms. The investigation was commenced in April 1938 and completed in March 1941. Altogether 84 animals were observed, 23 on A diet and 61 on diet B.

Observations —No significant differences in the state of nutrition of two groups were observed during the first few weeks. But as the experiment progressed, striking differences were noted in the health and well being of the two groups. Those of the animals in group A increased steadily in weight, while in group B they declined or remained stationary. The condition of the animal in group A was generally satisfactory, they were active and ate their food well, some animals in group A, survived for over two years in good condition. In general they remained fairly free from disease. Some animals suffered from relatively mild attacks of Diarrhoea from which they recovered easily. The monkeys in group A, when out at exercise, were active and playful compared to those in group B, who were listless and lost energy and much of the normal simian interest in their surroundings. On approaching the enclosure it was usually possible to distinguish from a distance of about 25 yards which group was out at exercise, from the behaviour of the animals. Group B animals, fed on the rice diet became progressively weak and died within 6 or 8 weeks, others survived for 6 to 12 months. In animals surviving for several months, a fairly constant clinical picture made its appearance, though there was much individual variation as to the time of onset. The appetite was impaired and attacks of diarrhoea occurred. The stools were small, pale in colour, and varied in number from 4 to 10 per day, microscopic examination of the stool revealed undigested food particles, degenerating epithelial cells and large number of bacteria. Mucous and blood were not present. In untreated cases, the animals usually became worse and died. As the aim of the experiment was to study the effects of chronic diet deficiency, supplements of milk (100 cc), sprouted gram (100 g) and one ripe plantain a day were given to some monkeys with diarrhoea, in addition to the basic diet, for a few weeks at a time, the object being to extend the period of survival. In animals which had not been fed for prolonged periods on the deficient diet and were in a fairly good general condition, the provision of these supplements usually checked the diarrhoea. The supplements were withdrawn as soon as the condition of the animal

improved. As the period on the deficient diet increased the attacks of diarrhoea tended to become more frequent and prolonged until finally a condition of chronic diarrhoea, leading to emaciation and death, supervened in many animals in the group. In the latter stages of the disease the supplements were without effect in checking the diarrhoea and improving the general condition. The incidence of attacks of diarrhoea in group B was about three times as great in group A. The average duration in days of each attack of diarrhoea was considerably greater in the former. During certain seasons both groups suffered from dysentery, but animals in group A usually got over the attack quickly, in group B it showed a tendency to pass into the sub-acute or chronic stage.

In addition to the gastro-intestinal disorders, some animals in group B showed signs indicative of deficiency diseases. These included catarrhal ophthalmia, xerosis of the conjunctiva, blepharitis, lacrymation, swelling of the eyelids, pyorrhoea alveolaris, spongy and bleeding gums, ulceration of the gums, wrist drops, spastic and flaccid paralysis of the limbs and chronic ulcers on the hind limbs. Two conditions, disorders of skin and oedema, were important. The hair became coarse, sparse and 'staring'. Some chronically deficient animals showed symmetrical denudation of hair over both hands and feet. The skin in these areas was rough and scaly and showed hyperpigmentation and branny disquamation. The condition was in some degree suggestive of cutaneous manifestation of pellagra. The tail also showed similar changes, in addition, chronic indolent ulcers were frequently present, especially over the feet. A few animals showed oedema which was peculiar in its onset and distribution. The oedema tended to appear suddenly, usually over the lower part of the face. It also involved the scrotum. Some monkeys showed swellings of hands and feet. The addition of supplements usually cleared up the oedema. The neurological manifestation and oedema were more marked in animals fed on raw milled rice which has a much lower Vitamin B₁ content than parboiled milled rice. These animals usually went down-hill rapidly and none survived for more than 23 weeks. The terminal clinical picture was one of great emaciation, marked prostration and chronic diarrhoea. The various lesions of the skin, eyes and gums described above and oedema did not occur in group A.

Autopsy findings —A complete post-mortem examination was carried out on 15 animals in group A and 40 in group B. Most of those from group A examined were killed in healthy state. In group B, the animals were killed when moribund. Pieces of tissues were taken for histo-pathological study as soon after deaths as possible to avoid post-mortem changes. The following description applies in general to the chronically deficient animals in group B. The animals were much emaciated and the face had a pinched appearance. One animal showed aphthous ulceration of gums. In

the abdomen there was very little subcutaneous, retroperitoneal or omental fat. Distension of the stomach and intestines was occasionally noticed. The omentum and mesentary were thin. The mesenteric and ileo-coecal glands were enlarged. The lungs were found collapsed and pigmented, the heart was smaller in size than normal, the internal appearances of the gastro-intestinal tract were interesting. The tongue was normal in most of the cases. The mucous membrane of the pharynx, oesophagus and stomach was pale. In the stomach it was thinner and in some cases it showed superficial erosions and petechiae. The duodenum was catarrhal and the mucosae were lined by thin layer of mucus. No ulcers were present. The jejunum and ileum showed varying degrees of atrophy. This being more marked in the lower part of the ileum, from about 10 to 12 inches above ileo-coecal valve downwards. The mucous membrane of the gut was soft, oedematous and lined by a layer of thick mucus, transverse folds were not prominent in the jejunum and were entirely lost in the lower ileum. In the latter, the atrophic Peyer's patches were rendered very prominent by the atrophic changes in the mucosa. The muscular layers also showed varying degrees of atrophy and in a well marked case, the ileum looked papyraceous. Instead of showing the normal pinkish appearance of the gut as seen in transmitted light, the ileum was palish-white in colour. Petechial haemorrhages were present in the small intestines in a few animals. The mucous membrane of the large intestine did not show similar atrophic changes. Evidences of acute, sub-acute, or chronic bacillary dysentery were present in the large gut in the animals which had suffered from disease. The liver was atrophic, the kidneys were pale and other internal organs showed no noteworthy microscopic changes. Gross gastro-intestinal lesions of the type described above were not met within group A.

Histopathology of the gastro-intestinal tract (1) Group B. Epithelium of tongue and oesophagus was normal. The mucosa of the stomach showed lymphocytic infiltration of the superficial parts of the mucosa, atrophy of gastric glands, serial sections of the intestines of animals surviving for varying periods on the deficient diet were examined. In animals fed on the rice for about 10 weeks the epithelium covering the villi showed degeneration. The lymphoid elements were reduced in number. In cases surviving for longer periods, the villi were almost acellular, with the covering epithelium lost. These appearances were similar to the 'withering of the villi' described by Mackie and Fauly in sprue, specimens removed from animals suffering from prolonged diarrhoea showed flattening of the villi and decrease in recticular tissue. In these cases mucous membrane was only few cells deep. The degenerative changes occurred in glands of Lieberkuhn. It is interesting to note that at no stage were inflammatory changes observed in the mucosa or submucosa. The submucous coat showed dilated congested vessels with petechial haemorrhages. The essential change

in the muscular coat of the small intestine was atrophy, the serous coat showed no abnormality. Degenerative changes of varying degree to the extent of complete atrophy were present in Auerbach's plexus. Changes characteristic of subacute or chronic bacillary dysentery were observed in the large intestines in some cases. The large intestine showed no evidence of the marked atrophic changes noticed in the small intestine. Group A. The atrophic changes in the small intestine described above were not evident in group A.

Haematological findings. Complete haematological investigations were carried out on all animals in both groups. Some animals in group B showed slight secondary anaemia, a few developed marked hypochromic, microcytic anaemia. Macrocytic hyperchromic anaemia was not observed in a single instance in animals fed on the deficient diets for prolonged periods. Smears taken from the bone-marrow showed a normoblastic reaction in cases with secondary anaemia. A megaloblastic reaction of the bone marrow was not observed in any case. Fractional test meals, showed a high incidence of hypochlorhydria in the stomach.

In his discussion the author notices two types of change in the gastro-intestinal tract of monkeys fed on the rice diets. The changes in the small intestine were degenerative in nature and non-inflammatory. On the other hand the lesions of the large intestine were inflammatory in type. Both groups of animals were kept under the same environmental conditions, the only difference being the diet given. It seems clear that the atrophic changes found in the small intestinal tract in group B were due solely to the deficient diet. While the intestinal condition dominated the clinical picture, group B in general showed multiple signs of deficiency diseases, these were due to the diet being deficient in many essential food factors. The presence of multiple haemorrhages in different organs, suggests a state of subclinical scurvy. On the basis of the observations recorded, however, the intestinal changes cannot be ascribed to deficiency of any particular vitamin or food constituent. The author thinks that further work is necessary to establish any such association. The author quotes a paper in the "East African Medical Journal" by McKenzie recording a clinical condition occurring in African labourers subsisting on very poor diets which appears to be almost identical with that observed in the monkeys, the name "nutritional diarrhoea" was given to this condition. The gastro-intestinal symptoms and the microscopic appearance of the gut in these cases were closely similar to those described above. McKenzie has noticed that incidence of 'nutritional diarrhoea,' among labourers fell remarkably with an improvement in the diet and living conditions on the estate. The author points out that the high incidence of gastro-intestinal disorders, particularly diarrhoea and dysentery in India and the increased death rate due to these causes in times of famine are well known. It is to

is observed that the death rate from 'dysentery and diarrhoea' in Punjab as recorded in the Annual reports of the Public Health Commissioner with the Government of India is usually from one-fourth to one-sixth to that of Orissa, the Central Provinces and Madras where rice is the principal or important staple diet

In the original article, the author has given a number of photographs of the animals and micro-photographs of the sections of tissues
J C P

TREATMENT OF THE NEPHROTIC SYNDROMES WITH SERUM TRANSFUSIONS

There are several factors upon which oedema in cases of Nephrotic Syndrome depends, hypoproteinaemia being the most important factor. Epstein based his treatment of high protein diet on the theory that hypoproteinaemia was due to loss of protein in the urine and that protein intake is not sufficient for this loss. H. Brown et al. (H. Brown, E. H. Gray, and P. L. Mollison, *Brit Med Jour* 1942, I, 515) tried the effect of transfusion of concentrated serum containing large amount of protein in the treatment of nephrotic syndromes. Of 12 patients treated, 8 were considered to be cases of Bright's Disease in the nephrotic stage. In the ninth case a diagnosis of lipoid nephrosis was made and in the tenth amyloid nephrosis. The eleventh and twelfth cases were examples of malabsorption of protein from the alimentary tract. The reconstituted serum from dried product was used in majority of cases. Protein content of the fluid injected was 18 to 23.9% in most of the cases. It was administered by syringe in cases of small transfusions of 50 to 200 cc taking 10 to 30 mins and by blood transfusion bottle in cases of larger amount (300 to 500 cc) taking up to 3 hours over the administration. Dosage ranged from 10 to 15 gm of protein in children and from 20 to 100 gm in adults and more than one transfusion of these amounts were given in most cases.

Of the 11 oedematous patients only cases Nos 3 and 4 were completely relieved of their oedema following serum transfusion. In case 3, however, oedema had returned within 10 days and this oedema was unaffected by a further transfusion of concentrated serum. In cases Nos 6 and 10 there was a slight reduction in oedema. In 5 cases there was no effect and in cases Nos 1 and 8 oedema increased after transfusion. Immediately after transfusion serum protein was generally found to have risen and the haemoglobin to have fallen. 24 to 48 hours after transfusion, however, the serum protein concentration was usually scarcely greater than before transfusion, and haemoglobin had usually returned to the pretransfusion level. This failure to produce an increase in serum protein cannot have been due to loss of protein in urine of cases examined. It appeared that the amount of albumin passed in the urine was not sufficient to account for the failure of serum proteins to increase. Of the

12 patients, suffering from oedema in only 2 was good diuresis produced and in one of these the oedema returned within 10 days and failed to respond to a further transfusion. From the results it appears that in the nephrotic stage of glomerulonephritis a transfusion of concentrated serum is as likely to be followed by an adverse as by a favourable effect. It has been suggested by the authors that concentrated serum is concentrated with regard to salts as well as protein and that, therefore, a considerable amount of salts is administered when a transfusion of concentrated serum is given. This may be an important factor in the prevention of diuresis. If it were possible to obtain by sterile dialysis a protein solution free of salts the resulting fluid might prove of greater value.

J C P

THE INDIAN PHYSICIAN

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VOLUME I

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NEW QUEEN'S ROAD BOMBAY

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Original Contributions

LUNG ABSCESS

By

M D MOTASHAW

M B B S

(From King Edward Memorial Hospital,* BOMBAY)

It is proposed in this paper to study from a clinical point of view, all the cases of lung abscess admitted to the K E M Hospital, Bombay, during the period, 1st January, 1939 to 30th June, 1942. There were 51 cases of lung abscess during this period and analysis of these cases is given below.

By lung abscess is meant a localised collection of necrotic tissue in the lung parenchyma which is neither tubercular nor bronchiectatic in nature and following this definition the cases of tubercular cavitation in the lungs were not taken into consideration in this series. Again, gangrene of the lung had to be differentiated from abscess of the lung, though the difference is only one of a degree or extent of the damage produced and no definite rule can be laid down to differentiate between the two. For all clinical purposes, those cases where the body resistance has failed to localise the process of necrosis to a part of the lobe of the lung, and allowed it to spread beyond this limit, and where the process is an acute fulminating one and where toxæmia is marked, the case can correctly be labelled as one of gangrene of the lung. Such cases were not included in this series.

During the three-and-a-half year period under review 51 cases of lung abscess were treated as in-patients in the K E M

* Hassanji Ranchodji Desai Prize Essay.
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Hospital Bombay During that period the total number of in-patients treated in the hospital was 43,765 so that lung abscess cases formed 0.119 per cent of the total admissions to the hospital or in other words for every 858 cases admitted to the hospital there was one case of lung abscess. The yearly incidence of lung abscess is shown in Table 1.

TABLE 1 Showing percentage incidence of lung abscess to total admissions

Year	No. of Admissions	No. of Cases	% of Cases
1939	11,921	11	0.093
1940	12,571	15	0.120
1941	11,115	20	0.174
1st Half of 1942	6,123	5	0.082

Mode of review

All the history-sheets were gone into and from the evidence available there each case was reviewed according to the case-sheet shown below.

CASE SHEET

DIAGNOSIS — Lung abscess

AGE — SEX — Male Female Child

Date of Admission

OCCUPATION COMMUNITY

Date of Discharge Expired —

No. of Days in the Hospital

Aetiology

1. Predisposing —

- (a) General debility
- (b) Malnutrition
- (c) Alcoholism
- (d) Diabetes
- (e) Syphilis

2. Exciting —

(A) Infection —

- (a) Post-operative
- (b) Sepsis in upper respiratory tract
- (c) Foreign body

(B) Respiratory Infections —

- (a) Lobar pneumonia
- (b) Broncho pneumonia
- (c) Respiratory Catarrh or "Influenzal Pneumonia"

(C) Embolic —

- (a) Pyaemia
- (b) Septic endocarditis
- (c) Otitis media
- (d) Phrombophlebitis
- (e) Puerperal Sepsis
- (f) Amebiasis

(D) Contiguous —

- (a) Mediastinitis
- (b) Malignant neoplasms of
 - (i) Tongue
 - (ii) Bronchi
 - (iii) Lung
 - (iv) Oesophagus
- (c) Cures of
 - (i) Ribs
 - (ii) Vertebrae
- (d) Impyema
- (e) Liver/or Sub diaphragmatic abscess

(L) Trauma:

- (a) Penetrating wounds of the lungs
- (b) Fractured ribs

(1) Undertimmed or Primary abscess of the lung

No of Abscesses (a) Single
(b) Multiple

Site —Right upper/middle/lower/lobe
Left upper/lower/lobe

Onset —(a) Sudden Insidious
(b) When were the symptoms first noticed after the primary or the antecedent condition?
(c) Was any Sulphanilamide used in treatment of antecedent condition?

Duration —The interval between commencement of the treatment and noticing the symptoms directly referable to the abscess

Symptoms — (a) Cough
(b) Expectoration —
Amount slight/profuse' slight alternating with profuse
Colour white/yellow/green/bloody
Smell foul
Layer formation Lung tissue Elastic fibres
(c) Fever (i) Intermittent or Remittant
(ii) Recurrent
(iii) Irregular
(d) Pain (i) Localised to a particular area of the chest
(ii) All over the chest
(e) Haemoptysis
(f) Dyspnoea
(g) Other symptoms

Signs — (A) General

- (a) Fever —
- (b) Clubbing of fingers
- (c) Enlarged spleen
- (d) Wasting

(B) Local

- (a) Vague signs of congestion
- (b) Suspicious
(i) Consolidation —
- (ii) Cavitation —

Laboratory Investigations —

- (a) Sputum
 - (i) Appearance Mucopurulent / Rank pus / Three layered
 - (ii) Quantity per 24 hours
 - (iii) Microscopic
 - Tubercle bacilli
 - Other organisms
 - Spirochaetes
 - Bacillus Fusiformis
 - Fungi
 - Elastic tissue
 - (iv) Cultural examination
- (b) Blood (i) Total white blood cell count
(ii) Differential white cell count
- (c) Kahn or Wasserman reaction of blood serum
- (d) Stool for vegetative or cystic forms of Entamoeba Histolytica
- (e) X ray Plate of chest (a) plain showing
(i) Vague opacity or consolidation
(ii) Cavity with fluid level
(b) after lipiodol cavity filled/not filled

Associated Diseases:

Treatment (a) Non-operative

- (i) General
- (ii) Postural
- (iii) Specific
 - (a) Fmetine
 - (b) Sodium Benzoyl intravenous
 - (c) Alcohol—intravenous
 - (d) Arsenicals
 - (e) Sulphapyridine
 - (f) Autovaccine
- (iv) Short wave diathermy

(b) Operative—

- (i) Artificial pneumothorax
- (ii) Bronchoscopic aspirations
- (iii) Phrenic evulsion
- (iv) Extrapleural compression
- (v) Pneumotomy and drainage one stage/two stage
- (vi) Lobectomy
- (vii) Thoracoplasty

Complications — (a) Dry pleurisy and thickened pleura
 (b) Empyema or Pyo Pneumothorax
 (c) Pericarditis
 (d) Mediastinitis
 (e) Congestive Cardiac Failure
 (f) Metastatic abscesses in brain/kidney/muscles
 (g) Meningitis

Sequelae — (a) Pleural adhesions
 (b) Fibrosis of the lung
 (c) Bronchiectasis

Result — (a) Cured radiologically
 (b) Relieved symptomatically
 (c) No improvement
 (d) Died

Post-Mortem — if any

Age The youngest age at which the abscess was seen in the present series was 11 years, while the oldest case was 55 years old. Almost 86% of cases were between the ages 21 and 50. The maximum incidence in the 10 year-group being between 21 and 30 years. The details of the age incidence can be seen in Table 2.

TABLE 2—Age Incidence

Age	No. of Cases	%
11-20	5	9.80
21-30	18	35.30
31-40	16	31.40
41-50	11	21.58
Over 50	-	3.92

On plotting a curve of the age incidence in lung abscess, we find that the curve shows a steep rise and a fall which is gradual in its early part, but steep later on. This curve corresponds in form to the curve of age incidence in respiratory infections.

Sex. In the present series there is a definite preponderance of males over females. Out of a total 51 cases, 42 were males and 9 were females. But this is not enough for our purpose because these figures are taken from a hospital where there is a definite preponderance of male attendance over the female attendance and so an attempt is made to compare the relation of male cases to that of male and female admissions into the hospital as shown in Table 3.

TABLE 3—Sex Incidence

	Total	Male	Female	Male %	Female %
Cases	51	42	9	82.35	17.65
Admissions	43765	31721	12044	72.73	27.27

The annual sex incidence shown in Table No. 4 is fairly constant and compares favourably with the collective sex incidence except for the fact that the incidence of females is slightly higher in the year 1939.

TABLE 4—Sex Incidence Year by Year

Year	Males	Females	Male%	Female%
1939	8	3	72.73	27.27
1940	13	2	86.66	13.33
1941	14	3	85.00	15.00
1942	4	1	80.00	20.00
Total	42	9	82.35	17.65

From Table No 3 it is seen that the incidence of lung abscess is slightly higher in males than in females. Though the percentage of female admissions was 27.27 of the total admission, lung abscess, was present in 17.65% of the total cases whereas the percentage of male lung abscesses is higher than the percentage of male admissions.

Community There is a negligible preponderance of lung abscess amongst Mohammedans over the other communities as shown in Table 5.

TABLE 5—Incidence of Lung abscess in different communities

Community	Cases		Admissions	
	Number	%	Number	%
Hindu	36	70.60	30085	68.42
Mohammedan	10	19.60	6766	15.91
Christian	4	7.84	5896	13.40
Others	1	1.96	1018	2.27
Total	51	100.00	43765	100.00

Occupation Most of the 42 males were either factory hands or mill hands working in a stagnant atmosphere. 3 were tailors who probably had to work in a stooping position for several hours a day. 3 were classed as coolies and 7 were unemployed.

Aetiology

Predisposing Causes Malnutrition, alcoholism, diabetes and syphilis are as much the predisposing causes of lung abscess as of any other disease and the investigations of these 51 cases show that there is no statistical evidence to condemn them and yet in the absence of properly worked out figures we cannot even acquit them. One feels that especially alcoholism or syphilis may be proved to co-exist with a fair number of cases of lung abscess because the age incidence curves of the ardent devotees of Bacchus and Venus correspond closely to the age incidence curve of lung abscess, but how far can these two conditions be held to be responsible for the actual preparation of the soil for a lung abscess to be formed one cannot say. Similarly, it was very difficult to judge how far malnutrition had helped the formation of lung abscess, for

though most of the cases that came to the hospital appeared ill-nourished, we could not say whether the malnutrition was the cause or the effect of the lung abscess. Similarly, there is no evidence to prove that diabetes predisposes a patient more towards the formation of a lung abscess than an abscess anywhere else in the body. In this series under review only one out of the 51 cases showed diabetes and only two had acquired syphilis. Hence it seems that they are not any more responsible for the causation of a lung abscess than of any other disease.

Etiologic Causes The causes as found in order of frequency in the present series are shown in detail in Table 6 below.

TABLE 6 - *Etiology*

Cause	Number	%
Respiratory Infections	17	33.33
Aspiration	1	1.96
Amoebiasis (embolic)	1	1.96
Otitis media (embolic)	1	1.96
Puerperium (embolic)	1	1.96
Extension	1	1.96
Undetermined or Primary	25	49.01

In the present series the most common individual cause of lung abscess was respiratory infection which accounts for as many as 33.33% of the cases. I, particularly say respiratory infection and not pneumonia because from the history available it was very difficult to be sure that the respiratory infection was genuine lobar pneumonia. Usually, the patients gave a history of 5 to 9 days fever of sudden onset accompanied by cough and expectoration. But, quite as many as seven out of these seventeen patients said that their doctors had made a diagnosis of pneumonia. Out of the remaining, two patients had been treated for pneumonia in the K E M Hospital and their old papers could not be traced.

The next largest group that accounted for as many as 9.80% of the cases was the embolic group. Cases where puerperium and otitis media were the causes were straight cases but the amoebic cases require some explanation. In these three cases there was no other cause evident for the lung abscess but they showed hepatitis and the stool examination showed cystic forms of *Entamoeba histolytica* and, therefore, a conclusion was, I believe justly, drawn, that emboli from amoebic abscesses in the colon were responsible for the lung abscess.

The third group was that of aspiration or inhalation abscess which accounted for 5.88% of the cases. Of these three cases, one was of a fungating epithelioma of the cheek which was subjected to diathermy-cooking and resulted into an abscess 8 days later. Another was of an inoperable carcinoma of the posterior one-third of the tongue extending downwards to the epiglottis. The third one was a case of definitely septic teeth with a lot of sloughing off of the gums.

A solitary case was accounted for by the process of extension of a carcinoma of the oesophagus penetrating into the lung.

In the remaining 25 cases, i.e., 49.03% no satisfactory cause could be found to explain the presence of lung abscess and hence they were labelled as cases of primary lung abscess.

The results of this series once again show that the post-operative inhalation or aspiration abscess is not the commonest type of lung abscess—at least not here, though it is so often mentioned by the western authors. Fisher and Finny are of opinion that as many as 28% of the lung abscesses are of post-operative origin, while Singer and Graham attribute 32% of cases of lung-abscess to post-operative inhalation. Lord in his series of 227 cases ascribed 33.33% to operations whereas Sweet raised that figure as high as 68%. Tonsillectomy is blamed the most for these high figures and the removal of adenoids, operations on the nose and the extraction of teeth help to swell the list. In Sweet's series tonsillectomy was responsible for as many as 44% of cases of lung abscess and in most, though not all, the operation was performed under a general anaesthetic. But, as Boyd explains, it is difficult to exclude the possibility of a septic thrombosis and embolism in these cases and after all they may not be bronchogenic in origin.

In the K. E. M. Hospital about 800 tonsillectomies are being done annually yet in this series there is not a single case recorded.

A mention may be made here of a case which evidently developed a post-operative lung abscess in the K. E. M. hospital, but has not been recorded in this series because it ultimately turned out to be of tubercular origin. A Mohammedan male aged 23, was subjected to a lateral rhinotomy, after a preliminary ligation of the carotid, for multiple nasal polypi. On the

fifth day after the operation he complained of severe pain in the right mammary region and could not rest without strong sedatives. Two days later he developed fever, which was of intermittent type, and started coughing. Five days after this he developed signs of consolidation in the right middle lobe and started coughing out blood-stained, foul smelling, sputum in large amount. A diagnosis of post-operative lung abscess was made and an x-ray plate was taken. The plate showed a cavity with fluid level at the apex of the right middle lobe with surrounding infiltration. The opposite lung was quite clear. His sputum was repeatedly examined by ordinary and concentration method for about 20 times and no tubercle bacilli were seen. He was discharged relieved, after a stay of 68 days in the hospital, but he came back three months later and on screening, showed three cavities in the right middle lobe without fluid levels. This time a routine sputum examination showed a large number of tubercle bacilli. Hence this case was considered to be one of pulmonary tuberculosis where the lesion was not open but the formation of a post-operative lung abscess helped the destructive process and made the case an open one in a due course of time.

Onset

The onset was insidious in all the cases except two and the patient took some time to find out that there was something wrong with himself or herself. In the two cases which formed the exceptions to this rule the lesion was of a fairly rapid onset, the periods being three and six days respectively.

Duration

The interval between the presence of the first symptom ascribable to the disease and seeking of medical advice varied over a long range. The minimum period was three days while there was a stoic who waited for four years before he came to the hospital.

When were the symptoms first noticed after the primary or the antecedent condition? This was a difficult question to answer in most of the 26 cases of known primary condition. Firstly because the onset was very insidious and patients could not say when the condition started, and secondly, the patients did not seem to have a good memory for their past diseases, yet their word has been taken for what it is worth and the fol-

lowing result arrived at In the 17 cases of respiratory infections the earliest onset was 10 days after the temperature had come down while the longest period was of 12 months In six cases the onset of the abscess was within 3 weeks of the primary infection, in four cases it was between 3 and 6 weeks, in two cases it was between 6 and 12 weeks and in five cases it was more than 12 weeks This is seen from table No 7

TABLE NO 7

Weeks No of Cases	0 3 6	3 6 4	6 12 2	More than 12 5
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In the embolic case which followed a delivery, the abscess occurred 20 days after the delivery

The case which had otitis media developed the abscess while he was taking treatment for his primary condition

In the case of aspiration abscesses the patient who had carcinoma of the posterior-third of the tongue developed the abscess 8 months after he had been informed of the growth, whereas the patient who had epithelioma of the cheek for 6 years developed an abscess 3 days after the epithelioma was subjected to diathermy cooking The third case was of septic teeth and here it was not possible to say how long he had that condition

Similarly it was very difficult to say when the patients acquired amoebic infection or when the carcinoma of the oesophagus started penetrating the lung tissue

Was any sulphonamide used in primary respiratory condition

This would have been a very interesting point to investigate but unfortunately no information regarding it could be found in any of the case-sheets and so this point had to be entirely abandoned Yet, if even now this point is carefully investigated in all cases of lung abscess coming to the hospital after this, I believe, we can gather very important evidence to support or refute the statement which is very often made, but is not yet statistically supported, that the incidence of the lung abscess has increased after the use of sulphonamide

But from our investigations it is shown that the annual incidence of lung abscess had gradually increased from 1939 to

1941 and this is also the period when the use of sulphapyridine has been constantly increasing. Of course, I do not make bold to say that this proves anything, I agree that looking to the figures of just three years is not enough and also that there may be other causes, like increase of respiratory infections and diminished mortality from respiratory infections which may partly explain this evident rise in incidence of lung abscess but I certainly say that this is a piece of evidence which may prove to be of value in some future investigations at a later date, if properly evaluated in connection with other data.

Symptoms

The symptoms of lung abscess are very suggestive and occur with a fair amount of constancy which justifies our suspecting the presence of an abscess from the history alone and very often guide us to make a fairly accurate diagnosis from clinical examination, without the aid of complex laboratory investigations, where a clinical examination alone could not have given us the least idea of what the underlying condition could have been.

The most common symptom was cough with a variable amount of expectoration. These two symptoms were found in 100% of cases. The other symptoms are fever, pain, foul smell, haemoptysis and dyspnoea and the relative constancy with which they occurred is shown in table 8.

TABLE NO. 8 -Relative frequency of symptoms

Symptom	No	%
Cough	50	100
Expectoration	50	100
Slight	6	12
Profuse	44	88
Slight alternating with profuse	5	10
Pain	50	100
Local	41	82
General	9	18
Fever	47	94
Intermittent	31	62
Recurrent	5	10
Irregular	11	22
Foul Smell	42	84
Haemoptysis	20	40
Dyspnoea	11	22
Frequency of stools	2	—
Dysphagia	1	—

Note -For the consideration of symptoms one case, which was admitted in a moribund condition and could give no previous history and no other person was available who could give his history has not been considered.

It is interesting to note that as many as 82% of cases had local pain which, though not confined to the exact spot over the abscess, was very helpful in suggesting the side of the abscess.

Fever was also a very constant feature, only 3 cases being afebrile in this series

Another important observation made is that as many as 40% of cases had haemoptysis which shows that haemoptysis is not as uncommon as it is made out to be. If taken in consideration with bronchiectasis, it shows that all that is cough and expectoration with haemoptysis is not pulmonary tuberculosis, as is often made out to be.

Dyspnoea was found in 22% of the cases but it had no particular characteristics by which it could be differentiated from dyspnoea due to other causes.

Signs —There are no definite signs by which a lung abscess can be diagnosed. The general signs are pyrexia and clubbing of nails, while the local signs may vary from the vague signs of congestion like impaired note and diminished air entry to the classical signs of excavation. In our series pyrexia was present in 48 cases and in most of these the temperature was intermittent or remittant in type. In spite of the fact that most of these cases were of a fairly long duration clubbing was noticed in only 6 cases. In 19 cases the local signs were vague and indeterminate while other 19 cases presented signs of consolidation. In 13 cases the abscess could be localised by signs of excavation over the affected part. The details of the signs are shown in table 9.

TABLE 9—Relative frequency of signs

Sign	No	%
Pyrexia	48	94.1
Clubbing	6	11.76
Vague	19	37.24
Consolidation	19	37.24
Excavation	13	25.49
Enlarged Liver	1	—
Enlarged spleen	2	—

Number of Abscesses —In 47 cases out of this series the abscess was a single one while in the remaining 4 cases multiple abscesses were seen. It is worth noting that in no case which has been described to be of embolic origin were the abscesses multiple. In three cases which showed multiple abscesses the cause was not determined while in the fourth case which showed multiple abscess the cause was an epithelioma of the cheek which had been recently subjected to diathermy cooking.

Site —The right lung was affected almost twice as frequently as the left one and in the right lung the lower lobe was affected more often than the upper one. The figures of this series are compared with that of a series of 125 cases reported by Sweet in the following Table —

Present Series				Sweet			
	Rt	Lt		Rt	Lt		
Upper lobe	No. 8	% 12.02	0	10.04	Upper lobe	% 21.09	0.60
		12.78					Upper lobe
Middle lobe	6		8	17.02	Lower lobe	15.2	20.8
Lower lobe	16	% 71.01			Middle lobe	29.6	
					Lower lobe		
Total	40	63.81	17	16.16	Total	69.6	30.4

The fact that a lung abscess is more common on the right side than the left, supported the theory that the most common cause was inhalation or aspiration, where the foreign material went down the right bronchus which is straight. But now it has been known from the study of cases of pulmonary embolism that embolism is also more common on the right side than on the left side. This statistical evidence knocks the strength out of the argument in favour of the inhalation theory.

Laboratory Investigations

The total and differential white cell count, the detailed examination of the sputum, the Kahn flocculation test, the routine examination of stool and urine and an x-ray plate of the chest were the investigations that were usually done.

Blood Count

This was carried out in 43 cases out of the total of 51. Of these 43 cases, 32 showed a leucocyte count over 8,000/cmm while the remaining 11 cases showed a count between 5,000 and 8,000/cmm. The maximum leucocyte count was 37,500/cmm while the minimum count was 5,000/cmm. A differential white cell count was also carried out in all these 43 cases. The number of polymorphonuclear neutrophils varied from a maximum of 88% to a minimum of 47%. One case showed 6% of eosinophils but that case had an associated bronchial asthma.

Sputum

The sputum, being the most important aid to clinical findings, was examined in all the 51 cases.

Quantity in 24 hours —The quantity of sputum was measured in 21 cases only. The maximum quantity noted in 24 hours for any case was 22 ozs and the minimum was 4 ozs.

Nature

The sputum of all the patients was collected in a conical glass and its naked eye description was noted. The sputum was mucopurulent in 10% of cases while 16% coughed out frank pus. In the remaining 74% the sputum settled down in three layers on standing which is the text-book characteristic of sputum in lung abscess or bronchiectasis.

Organisms The smears were as a routine examined for mycobacterium tuberculosis by ordinary as well as concentration methods and in all the cases such an examination was carried out more than three to four times at varying intervals. In no case were the tubercle bacilli seen. The other organisms seen in Gram's smears were most often streptococci, pneumococci and the micrococcus catarrhalis with the staphylococcus albus in a few cases and Gram negative bacilli in others.

The bacillus fusiformis was seen in only 3 cases. In no case were any fungi seen in the sputum. Unfortunately the spirochaetes were looked for in 9 cases only and were found in 2 of these. These figures do not corroborate the statement often made that the spirochaetes and the fusiform bacilli are very often the secondary organisms in lung abscess, but the number of cases investigated is not enough and no definite conclusion can therefore be drawn at this stage.

Elastic Tissue —This was seen in 5 cases only while in three others a note has been made that elastic tissue was not seen. In the other 43 cases no mention has been made of the presence or absence of elastic tissue.

X-ray —An x-ray plate of the chest was taken in 46 cases out of the 51 reviewed in this series. In as many as 38 cases (i.e. 82.61%) an abscess cavity with a fluid level could be clearly seen. In one case (2.18%) a dry cavity was seen while in the remaining 7 cases (15.21%) the x-ray appearance was vague in the sense that there was either an opacity or a consolidation or a picture suggesting dense infiltration.

A bronchogram after lipiodol was taken in four cases where the abscess cavities with fluid were seen in the lower lobes. Of these only two cavities were filled with lipiodol while in other two the oil could not enter the cavity. One of these four cases showed an associated bronchiectasis in the opposite lung.

Serological test for syphilis —Either the Kahn flocculation test or the Wasserman complement fixation test was carried out in 14 cases of the 51 and it was +++ in one and ++ in one more while it was negative in the remaining 12 cases.

Stool —The stool was examined in all the 51 cases and in three cases cysts of *entamoeba histolytica* were detected. These are the three cases where no other cause for the formation of the abscess could be determined and which were, therefore, considered to be of embolic origin from amoebic abscesses.

In one case blood was taken for culture but no growth could be obtained.

Associated Diseases

Besides the three cases who had malignant growths and three more who had hepatitis which were the immediate causes of lung abscess 7 cases had some other disease with the lung abscess as shown in the Table No 10.

TABLE 10 — Associated Diseases

Disease	No. of Cases
Aneurysm of aorta (syphilitic)	1
Bronchial asthma	1
Bronchiectasis	1
Broncho pneumonia	1
Diabetes	1
Pleural effusion	1
Syphilis	1
Total	7

Treatment

As this was not a preconceived investigation, no attempt was made to treat the cases on a particular line or in divided groups following different lines of treatment but one case was treated on more than one line according to the individual response of the case.

All the cases were treated along the general line with expectorant mixtures and antiseptic inhalations and their general hygiene and physical comforts were attended to as usual. 18 cases did not receive any other than this treatment with postural drainage.

The general and the postural treatments were supplemented by certain other special drugs like intramuscular or subcutaneous emetine, intravenous sodium benzoate and absolute alcohol, intramuscular or intravenous arsenicals, oral administration of sulphapyridine (M & B 693), subcutaneous autovaccine and short wave diathermy. As said above, any one case was given more than one of the above drugs.

Besides these non-surgical measures surgical treatment like artificial pneumothorax, external aspiration of the abscess, bronchoscopic aspirations and pneumotomy and drainage were also tried in a few cases. Other surgical aids like phrenic evulsion, extra pleural compression, lobectomy and thoracoplasty do not seem to have appeared suitable to the surgeons for the requirement of our cases.

A detailed statement of the number of cases receiving each type of treatment is shown in Table No 11.

TABLE 11—Treatment

Nature of treatment	No. of cases treated
General	51
Postural	49
Emetine	12
Sodium	11
Arseicals	10
Sulphapyridine	10
Alcohol	4
Short wave diathermy	24
Autovaccine	1
Artificial pneumothorax	1
External aspiration	1
Bronchoscopic aspiration	1
Pneumotomy and drainage (in 2 stages)	2

Duration of Treatment

If we exclude two cases which died within the first twenty-four hours of their stay in the hospital, the remaining 49 cases had an aggregate stay of 1514 days in the hospital before they were cured or relieved symptomatically or went away without any relief or succumbed to their disease. This gives us an average stay of 30.9 days in the hospital irrespective of the result obtained. The maximum individual stay recorded was of 131 days in a case which went home symptomatically relieved whereas the minimum stay recorded was 4 days where the patient went home against medical advice without obtaining any relief. The minimum period recorded during which a patient was symptomatically cured was 6 days while the minimum period required for the radiological cure of a patient was 22 days.

Complications

3 of these cases developed congestive cardiac failure and expired while 3 more had recurrence of symptoms, after being discharged symptomatically cured, within a period varying from 3 months to 9 months. One patient developed pyopneumothorax.

None of the other complications mentioned in the case-sheet were observed in our series.

Sequelae

As the follow up of our cases was very poor and few cases ever came again unless they had recurrence of the disease, no sequelae were noted.

Results

A case which was relieved of all its symptoms and showed no evidence of the disease radiologically is considered as cured (signified by letter C) while a case which was relieved of its symptoms yet showed some evidence of the disease, e.g., haziness was pronounced as relieved (signified by letter R). A case which showed only a partial improvement of symptoms or showed no improvement whatever or showed deterioration of its condition was signified by the letter O while those that succumbed to their disease were signified by the letter E. The detailed results are given in Table 12.

TABLE 12—Results

Result	No. of Cases	%
C-cured	6	11.76
R-relieved	24	47.08
O-no result	7	13.72
E-expired	14	27.44
Total	51	100.00

These results are compared with results of other authors in Table 13.

TABLE 13—Results of various authors

Authors	No. of Cases	C%	C+R	R%	O%	E%
Present series	51	11.76		47.08	13.72	27.44
Fisher & Finney	88		59.00		2.00	41.00
Neuhaff & Tournoff	45		88.89		6.67	4.44
M. J. Shah	50		42.00		18.00	40.00
Schlicphate	15	93.33				6.66

In the above series the treatment of the cases described by Fisher and Finney and M. J. Shah resembled the treatment

given in this series and the cases were unselected. In the cases described by Neuhauff and Tourhoff one stage pneumotomy and drainage was done hence this is a series of selected cases. Schliephate treated his 45 cases with Short wave diathermy and produced very good results as shown above.

The results of course depend upon various factors of the case. An attempt is made here to find out what are the factors which materially affect the result, i.e., the prognosis of the case.

The relation of aetiology to results is shown in Table 14.

TABLE 14—*aetiology in relation to results*

Cause	No	C%	R%	O%	E%
Respiratory Infections	17	5.88	52.93	17.65	23.54
Aspiration	3				100
Amoebiasis	3		73.33		66.67
Otitis Media	1				100
Puerperium	1				100
Carcinoma oesophagus	1				100
Primary	25	20.00	56.00	16.00	8.00

From Table No. 14 it can be seen that results of respiratory infections correspond very closely to the general results whereas the group classified as primary lung abscess has much better results. It may be perhaps that this primary abscess may be of the aspiration or inhalation type as suggested by some, the septic material coming from the mouth and teeth or that they may be embolic origin as suggested by Boyd. In any case they seem to be of lower virulence than others giving the best response to treatment.

The stage at which treatment is started also plays an important part in the prognosis as shown in Table No. 15. Here the results are compared against the interval elapsing between first noting the definite symptoms which could be ascribed to a pulmonary abscess and the starting of treatment.

TABLE 15—

Treatment started within	No of Cases	C%	R%	O%	E%
15 days	13	15.39	53.85	7.69	23.07
1 Month	22	9.09	54.54	13.64	22.73
6 months	12	16.67	25.00	25.00	33.33
1 year	2		50.00		50.00
4 years	1		100.00		

If we discard the last two columns where the number of cases is not sufficient to circumvent the normal curve of error and therefore of no statistical importance, we find that the prognosis goes on becoming more unfavourable as the starting of treatment is delayed. Here attention should be drawn to the

which of the special line of treatment is likely to benefit the patient most

A review of the type of this work cannot be expected to be of much use unless a preplanned campaign is followed and the cases are studied while they are there, on a uniform bases and different groups are given different lines of treatment which do not overlap one another. This alone will help us to study the merits and demerits of a particular line of treatment

Post-mortem findings

Out of the 14 cases that expired due to lung abscess a post-mortem examination could be done in 3 cases only. In two of these cases the cause was known antmortem and the clinical findings were confirmed. In the third one, an abscess with surrounding bronchopneumonia was seen but its aetiology could not be determined

Summary

- (1) An analysis of 51 cases of lung abscess admitted to the K E M Hospital during the last three-and-a-half-years is made
- (2) Majority of these cases are found to be between the ages of 21 and 40 years
- (3) Besides the primary or the idiopathic abscess, the most common cause is respiratory infection
- (4) Cough with expectoration, fever and foul smell to the breath or expectoration are the most important and constant symptoms
- (5) There are no definite physical signs of the condition
- (6) The right side is more often involved than the left
- (7) The x-ray plate shows an abscess cavity in a majority of cases
- (8) What was the best line of treatment could not be judged from the available data
- (9) The influence of aetiology and early treatment on prognosis is shown

(My very sincere thanks are due to the Dean of the K E M Hospital for permission to go through the records of the hospital and to the various members of the honorary staff who allowed me to record the cases under their care)

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THE DIAGNOSIS AND TREATMENT OF THE DIARRHOEAS

Diarrhoea is a frequent complaint in a variety of pathological and functional disturbances, sometimes a manifestation of some serious malady, sometimes only a passing disturbance, in many cases a symptom for which no cause can be found, but always a symptom which needs to be thoroughly investigated and treated early and strenuously. A physician who neglects this maxim is sure to find himself sooner or later in a humiliating position.

The investigation of diarrhoea requires a thorough clinical history. But only history is not sufficient. It can often be misleading. A complete physical examination of the patient, and a naked eye examination of the stools is necessary in all cases and a laboratory examination of the stools and a digital examination of the rectum in most cases and sigmoidoscopic or proctoscopic examinations of the lower bowel may be necessary in some cases. One would think very little of a specialist who treats tonsils, without looking at the throat, but one daily sees practitioners who are treating cases of diarrhoea without looking at the stools or without putting a finger in the rectum.

When a patient complains of diarrhoea it is necessary to ascertain what he means by it. In some, the complaint is of a number of watery stools per day, in others there are only one or two loose or mushy stools early in the morning, some complain of several stools per day consisting of small hard lumps of faecal matter, while others state that they have to go to the lavatory several times a day but are unable to pass anything. These latter have a fear of getting diarrhoea whenever they have to go out in public, to travel in a tram, bus or train or have to attend to some important business appointment or examination. Others complain of frequent stools consisting of blood-stained mucus with a desire to go to the toilet again, no sooner they come out of it.

The symptom of diarrhoea requires a careful analysis just as any other symptom. No assumption is warranted on the patient's mere statement. What do you mean by diarrhoea?

How often do you have to go to the toilet ? What are the stools like ? Liquid, semisolid, mushy, hard ? Amount, colour, smell, presence of gas, froth, blood or mucus, and tenesmus, all require careful enquiry. Most patients using modern toilets will give vague answers to these questions because they have not observed their stools or are not reliable witnesses and it will be necessary in every case to have a look at the stools. What time of the day do you get the frequency ? Mornings only or throughout the day ? Any relation to time of meals or nature of food ? Do you have to get up at night to pass a stool ? Can you think of any special circumstances associated with frequency of stools, e.g., emotional stress, changes in diet ?

As much detailed information as possible about the onset of diarrhoea should always be obtained. How did the diarrhoea begin ? What food did you have on the day or the day previous ? Did others share it ? Did any of them suffer from a similar complaint ? What treatment did you have the first time you had an attack of diarrhoea ? How soon after it did you start your normal diet ? Too soon after an acute enteritis, many patients are allowed a full diet, the intestinal mucosa is not given sufficient time to heal and a chronic state of ulceration or lack of absorption follows.

Do you have to wake up at night to pass a stool ? The answer to this question is very helpful. If the patient has to get up at night from sleep to pass a stool, most probably, he has acute ulceration of the colon, if not, he is more likely to have some type of the nutritional deficiency diarrhoea or the so-called functional diarrhoea.

Do you have tenesmus ? How urgent is the call when it comes ? The patient who can hardly wait and has to run to the toilet has most probably considerable ulceration of the rectum. There is much distress and tenesmus even after the bowels have moved. There may be dysentery or sometimes carcinoma recti.

Do you have bleeding piles ? The presence of these does not preclude the possibility of dysentery or of malignancy. In fact in the presence of congestion and inflammation of the colon, the piles are likely to get inflamed or bleed profusely. Before treating every case of pile the possibility of the colonic ulceration and malignancy should always be ruled out by digi-

tal and visual examination of the rectum, and if necessary the lower colon

Do you suffer from sore tongue or sore mouth? Burning tongue, especially the tip and the sides, soreness, ulceration of the oral mucosa, and inability to eat hot or spicy food are very frequent in sufferers from diarrhoea as a result of nutritional deficiency, sprue, tropical macrocytic anaemia, pernicious anaemia or pellagra. Sometimes the diarrhoea may precede the sore tongue by several months, in others it may be absent. In advanced cases the raw, red, angry, atrophied tongue is very characteristic. Repeated attacks of stomatitis should always lead one to investigate the dietetic habits of the patient.

Pigmentation, especially of the cheeks, forehead, palms of the hands and extensor surfaces of the forearms and legs, should also direct one's attention to tropical anaemia or pellagra.

Do you suffer from flatulence, borborygmi or marked abdominal distension? This is also a common symptom in tropical nutritional anaemia or sprue and may precede the diarrhoea by several months. The abdominal discomfort leads the patient to curtail or alter her diet, which further leads to nutritional deficiency and aggravates her condition.

Do you suffer from numbness in fingers, feet, or legs? Any paraesthesia? Cramps? The tropical nutritional anaemia is often associated with it, though frank nervous changes, altered reflexes, ataxia, etc., are only found in sub-acute combined degeneration associated with pernicious anaemia.

Have you lost any weight? Diarrhoea of any duration will produce loss of weight, and in some cases it will be extreme. It is not uncommon to come across cases of nutritional anaemia or sprue where the patient has lost 20 or 30 or even 50 lbs. of weight. If one finds that in spite of diarrhoea of some duration there is little or no loss of weight, then most probably the condition is due to some pathological changes in the lower end of the colon, or some functional disturbance or some poorly understood forms of diarrhoea. In early pernicious anaemia the loss of weight is not great.

Is there any evidence of endocrine disorders? Palpitations, tachycardia, tremors, thyroid enlargement, or eye signs should draw one's attention to Graves's disease, while marked pigmen-

after a bowel wash Hypogastric griping pain in the left iliac fossa, and digestive disturbances are frequently present The colon and the rectum may be loaded and the coecum distended It may be possible to palpate, indent and displace faecal masses on abdominal palpation There is no true obstructive peristalsis At times the diagnosis from carcinoma of the colon is very difficult In some cases of faecal impaction in the aged, there is a persistent diarrhoea with abdominal pain, and a complete abdominal and rectal examination, if necessary after several bowel washes, should never be omitted in any case of chronic diarrhoea Constipation is not an uncommon cause of diarrhoea in others also Faecal masses in the caecum set up a typhilitis and there is alternating constipation and diarrhoea The condition may be corrected by keeping the lower bowel clear with enemata of normal saline

True Diarrhoea

Nervous or Emotional Diarrhoea—Emotional stress is a frequent cause of diarrhoea In some patients the anxiety state may be easy to recognise, in others, who are ashamed of their state or who are not ready to recognise unconscious fear as a cause, it will require much ingenuity to make the diagnosis In some of these patients the "intestinal hurry" is so extreme that recognisable objects such as fruit particles or pips may be ejected per rectum a bare hour or even half an hour after taking it We should not ignore the statement of the patient that she passes some fruit or milk barely half an hour after she has taken it

Gastrogenous or achlorhydric diarrhoea In a certain number of persons with achlorhydria, gastric contents pass very rapidly to the colon and the stools contain undigested muscle fibres The diarrhoea is usually in the morning, the patient has to get up early in the morning, say 6 a.m. in order to pass a stool The condition is intermittent All persons suffering from achlorhydria do not suffer from morning diarrhoea In all cases of morning diarrhoea it is advisable to do the gastric analysis to find out if there is achlorhydria, and to put the patient on the dilute hydrochloric acid if he has no free acid If it is going to help him it will do so in a day or two The absence of free hydrochloric acid may suggest that the diarrhoea is an early symptom of primary macrocytic anaemia In a number of

states of nutritional deficiency, such as sprue, tropical anaemia, pellagra, pernicious anaemia, diarrhoea and achlorhydria are associated, and primary gastrogenous achlorhydric diarrhoea can never be diagnosed unless these deficiency states are completely ruled out

Food idiosyncrasy or Gastro-intestinal allergy is a frequent cause of diarrhoea. The diarrhoea is explosive, troublesome and may affect for several years before the offending article of food is found out. It may be necessary to keep a regular record of all the articles of food eaten before the bouts of diarrhoea. Milk, eggs, pulses, beans, chocolate are known to produce such intolerance. Where allergy is suspected, it is advisable to put the patient on a bland elimination diet, say on rice and buttermilk, for forty-eight hours. If this does not help, he should be given nothing by mouth except glucose water for two or three days. If this fails to check the frequency then perhaps nothing will. The cause is somewhere else.

Intestinal catarrh may result from drugs (arsenic, mercury, digitalis), food poisoning, chronic alcoholism, congestion of bowels, (cardiac disease or cirrhosis of liver), chronic nephritis, uraemia, or amyloid state and the diagnosis is not difficult, once the primary condition is recognised.

Tubercular diarrhoea. Diarrhoea is frequently present in incipient pulmonary tuberculosis, in advanced tuberculosis with ulceration of the bowel, in tubercular peritonitis and in tuberculosis of the suprarenal glands (Addison's disease). In the presence of pulmonary disease, the diagnosis is easy, but in its absence the diagnosis of intestinal tuberculosis is extremely difficult. Diarrhoea in abdominal tuberculosis is associated with pain. It is often intermittent. It may alternate with constipation. Ulceration of small bowel, caecum and ascending colon may not produce any diarrhoea, while ulcers in the lower segments of colon and rectum will often produce persistent diarrhoea, but not always, because the extensive ulceration may have destroyed the nerves and the state of the bowel may be such as to preclude all peristaltic activity. In these cases, there is constipation or even obstipation. The diagnosis of abdominal tuberculosis is always difficult. Examination of the gastro-intestinal tract after barium meal may help to determine the rate of peristaltic movement, the hurry or the stasis in the small bowel and the ascending and transverse colon. The exami-

nation of the colon after barium enema may be necessary to diagnose tuberculosis of the caecum or ulceration in the large gut. The finding of tubercular bacilli in the stools is of little diagnostic value

Suprarenal disease or Addison's disease is associated with marked pigmentation of the skin and mucosa, low blood pressure and marked asthenia. Insulin hypersensitiveness may be used in differential diagnosis. Effect of sodium chloride by mouth and D O C A injections may help

Colitis Perhaps the commonest cause of colitis is the habitual misuse of purgatives or irritant drugs or diet. Indigested food hurried through the small bowel will irritate the colon and set up a colitis. Primary ulceration of the colon also produces diarrhoea. In ulcerative colitis there is a persistent diarrhoea, without intermissions of constipation. The stools may contain blood,—sometimes free haemorrhage. The stools are soft chocolate brown, often streaked with blood and shreds of mucus or muco-pus. There is some abdominal pain, flatulence, and soreness over the colon. The sigmoid is palpable, thickened and tender. The x-ray examination after barium enema may show ulcer craters as patches retaining barium, variable filling of the bowel, dilatation of the lumen, absence of normal haustration and intermittent contraction giving the "string of sausages" appearance. Sigmoidoscopy may be necessary in some cases. It should not be done in acute cases. A swab taken from the ulcer may show some specific organism, streptococcus, or dysentery bacillus or amoebae. Often the bacteriological examination is inconclusive.

Chronic amoebic dysentery produces a clinical picture similar to this, and the diagnosis is made only by the stool examination for *entameba histolytica* or its cysts. In many cases of amoebiasis there is only simple diarrhoea and no dysentery. The stools are well formed and only two or three in the early morning. It is very easy to miss these cases. Conversely amoebic dysentery is often diagnosed when the condition is some other form of colitis or simple diarrhoea of some other cause. The presence of a few cysts in stools should not rule out the possibility of other causes of diarrhoea. One may treat these cysts if one likes but no one should be surprised if the diarrhoea persists and the patient does not improve. It will not

be wise then to poison him with courses of emetine and other similar drugs

Balantidium coli (ciliate dysentery) sometimes causes ulceration of the colon. The state is often latent and symptomless, but sometimes there are loose motions, with blood and mucus. Diagnosis is only possible by demonstrating *Balantidium coli* or its cysts in the excreta or in scrapings from the ulcers themselves. Sigmoidoscopy is required to see the colonic ulcers. In early and insidious cases there may be no blood and mucus in the stools but only loose stools, hence the importance of ciliate infestation in the differential diagnosis.

Flagellate Diarrhoea. Encysted cysts of the common intestinal flagellates are present in normal stools. Free flagellate forms only appear when the stools become liquid or loose. The intestinal flagellates—*Giardia intestinalis*, *Trichomonas hominis*, and *Chilomastix mesnili*—do not attack the intestinal mucosa, and most probably they are not pathogenic. However, *Giardia intestinalis* or *lamblia* is known to inhabit duodenum and jejunum and bile ducts and is associated with periodic attacks of diarrhoea, with passage of large quantities of clear mucus or ochre-yellow stools with a large number of free flagellates.

Schistosomiasis (Bilharziasis) and *Ascariasis* should also be remembered as causes of diarrhoea in some persons. Anaphylactic and toxic symptoms with fever sometimes may produce very confusing and varying pictures and at times much difficulty in diagnosis. If the search for ova in the stools fails therapeutic test may be resorted to.

Mucomembranous colitis is an intestinal neurosis and is better described as "Bowels on the Brain". The condition is commonly found in neurotic thin subjects, usually females, unmarried or sterile, of poor appetite, and always ailing. There are acute exacerbations from time to time. There is frequency of stools, with passage of much mucus or mucous casts of the bowel either complete or shreddy. Usually they suffer from much abdominal pain or discomfort, dragging or soreness, bouts of constipation, and a hoard of neurotic symptoms. The formation of casts may be due to allergy, to excessive secretion due to neurosis, their condensation into tubes or shreds due to slow bowel action. The state is well described as "intestinal asthma," and is often associated with bouts of migraine, eczema,

bronchial asthma, or spastic colon. The subjects are habitual drug takers for constipation or in the habit of taking regular enemas or bowel irrigations. The diarrhoea is in reality spurious. When the cast is passed, there is much colicky pain and tenesmus. When the cast or mucous shreds are seen, and the personality of the patient understood, there is no difficulty in the diagnosis. The variety, the wide-spread nature and the chronicity of the symptoms should warn one from making a diagnosis of focal organic lesions.

Spastic or Irritable colon is a similar condition of intestinal neurosis, a form of anxiety neurosis. Perhaps it may be taken as a minor aspect of mucous colitis. The patient is a vagotonic, introspective, highly strung type. Sometimes he may put on such a bold face that he appears just the reverse type as a tough guy, but underneath the mask, one can recognize the individual with a hyper-irritable neuromuscular apparatus. A little probing may reveal the hidden fears and anxieties. These prevent the regular motor activity, depending upon the orderly alternation of contraction and relaxation. Introspection, emotion, fears, "sex repression or starvation," susceptibility to the suggestions of disease such as carcinoma or appendicitis, phobias about constipation or intestinal toxæmia, faith in different 'paths' or nature cure, from time to time,—these make up the background. There may be some physical basis for the trouble at the beginning, a kink, an attack of dysentery, fever, or toxæmia, or the symptoms may be inverted sublimation of emotional crisis and needs. Some are sufferers from periodical paroxysmal headaches, bronchial asthma, or eczema. They will go any length to secure a cure and it is not rare to find a number of scars on the abdomen from previous operations. It is extremely difficult to convince them that the seat of their trouble is not in the colon but in the psyche. Sympathy is what they are after or at times perhaps revenge on some near or dear one.

Diarrhoea after Gastro-enterostomy Sometimes when the stomach is jointed to a segment of the lower part of the ileum, by some inexperienced surgeon, there is diarrhoea and oedema as a result of sidetracking of most of the small bowel. Similar state occurs when a patient who has gastro-enterostomy done and who had a gastro-jejunal ulcer, which has bored its way into the colon. He passes frequently undigested food and his mouth smells of feces. Barium enema will show that the ba-

rium enters the stomach through colon showing the gastro-colic fistula Diarrhoea here soon leads to nutritional deficiency and severe macrocytic anaemia and oedema

Coeliac disease of children (Gee's disease, or Herter's Intestinal Infantilism) is an ill-understood malady of childhood characterised by wasting and the passage of large, pale, offensive stools with an excess of split fat *Idiopathic Steatorrhoea* of adults called non-tropical sprue is a similar condition *Tropical sprue* or *psilosis* is also an allied condition of unknown aetiology, where there is an inability to absorb adequately fat, glucose, calcium, and vitamins There is associated achlorhydria in a large number of patients, and later on megalocytic anaemia, tetany, and avitaminosis There is typical morning diarrhoea with clay coloured, bulky, foul smelling, gaseous, fatty stools, and much wasting The inflammatory aphthous changes in the buccal mucosa and the tongue are very typical

Chronic pancreatitis is usually latent and only diagnosed at operations or post-mortem When the pancreatic function is sufficiently affected there may be diarrhoea with stools containing excess of fat and undigested meat fibres, with progressive emaciation and asthenia Glycosuria and hyperglycemia are not common in early cases Chronic progressive jaundice, with or without a history of gall stones should suggest chronic pancreatitis Diagnosis from catarrhal jaundice, gall stone, or carcinoma of the head of pancreas is often impossible even at the operation

Hill diarrhoea is a temporary disturbance of the gastrointestinal tract in persons going up the hills at elevations of 6,000 ft or over There is morning diarrhoea with abdominal distension and flatulence Defecation is urgent and generally occurs about 5 a m, there may be four or five stools before noon Stools are copious, frothy, pale and foul smelling The diarrhoeic condition resembles that of sprue and some cases develop frank sprue afterwards

Nutritional deficiency or defective diet diarrhoea is perhaps the commonest form of diarrhoea met with in practice There is sufficient clinical and experimental evidence to believe that a generally defective diet produces such changes in the mucous membrane of the gastrointestinal tract that there is lack of absorption of fat, glucose, minerals and vitamins, with the re-

sultant progressive emaciation, asthenia, general oedema, tropical macrocytic or microcytic anaemia, tetany and avitaminosis, as shown by changes in the buccal and lingual mucosa, cheilosis, changes in the eyes, skin pigmentation, and pellagrous dermatitis. Paraesthesia, neuritic pains, burning in fingers, toes and tongue, alteration in reflexes, neurasthenia and psychosis are not uncommon. Gross nervous lesions like those of subacute combined degeneration are not described. The diarrhoea occurring in *pellagra* and *Pernicious anaemia* has a similar aetiology.

In Hyperthyroidism or Graves's disease sometimes diarrhoea is a prominent symptom. In the presence of the eye signs and the enlargement of the thyroid, the diagnosis is not difficult. Where these manifestations are absent, in the so called cases of masked hyperthyroidism, the recognition of the condition is difficult. The patient is usually a nervous woman, sometimes a man, who complains of frequency of stools, as many as 8 to 12 per day. The stools are hard small lumps. There may be tachycardia and loss of weight. On careful examination one may detect minor signs of hyperthyroidism such as restlessness, staring expression, warm moist skin, some fullness in the neck, increased pulse pressure, rapid pulse and increased basal metabolic rate. If the colon is found to be palpable and tender and if a few cysts are found in the stools of such a person, it will not be wise to treat her for amoebic dysentery. The proper diagnosis and treatment will be for hyperthyroidism.

No cause found One must confess that in spite of a detailed clinical history and a thorough physical examination and laboratory investigation, in a large percentage of cases it is not possible to arrive at a diagnosis. All examination—stools, gastric analysis, barium enema, barium meal, sigmoidoscopy, blood count, basal metabolic rate—is negative. Such cases may probably be taken as due to nervous or psychic factors or perhaps as early functional stage of nutritional deficiency before actual organic changes have occurred in the gastrointestinal mucous membrane. A little probing in the personality of the patient and his dietetic habits will often repay the extra trouble.

Alvarez has repeatedly given warning which it is well for the profession to take to heart that minor pathological findings

should not be overstressed and ignoring other factors a diagnosis should not be based on them. A few ova or cysts in the stools, a congested throat, a deviated septum, or a septic focus somewhere should not lead one to attribute patients' complaints to amoebic dysentery, ankylostomiasis, tonsillitis, or to think that the high blood-pressure or diabetes or coronary sclerosis or asthma or osteoarthritis are due to septic absorption from a focus in the nose or teeth. It is wise to attend to these pathological findings, but there is no evidence to take them as causes of serious maladies. If amoebic cysts are found, it is best to give a course or two of antiamoebic treatment to see if the patient improves. To persist in it to the exclusion of other investigations is folly. One can harbour a number of these cysts on and off for years without any deleterious results. Again, it is quite impossible to make some persons cyst-free.

Treatment

In acute diarrhoea, if a patient has a number of stools it is wise to omit the customary castor oil. The intestines are irritated enough and probably there is little faecal matter left there to be ejected. A warm saline bowel wash will be useful to clear out the lower bowel. Plenty of fluid is required. If it cannot be taken by mouth, and if the patient is dehydrated, it should be given subcutaneously or intravenously. If there is any vomiting, glucose will be found useful. For a day or two or three it will be best to stop all feeds by mouth except water, Later buttermilk or curds and fruit juice—a non-residue diet—may be allowed. Apple juice or pomegranate juice is well tolerated. Of drugs, if there is much tenesmus tincture opii should be given in full doses. Kaolin is the drug of choice to absorb toxin, help solidification of stools and prevention of bacterial growth. In early cases it is best to give it in two teaspoonful doses every hour, then every two or three or four hours according to requirements. It may be combined with thirty grain doses of bismuth carbonate and calcium carbonate. No purgative should be given if the patient complains of constipation, because no food is given and the colon takes two or three days to fill up. A normal saline enema may be given if the patient asks for it. The food should be increased gradually and, rice, bread and vegetable purees, fruit such as over-ripe bananas, may be added. It is best to give rest to the inflamed bowels for a week or two and not to start on regular diet too soon, otherwise a relapse is likely to occur and a chronic state of diar-

diarrhoea may result For this reason for a long time, no irritating purgatives should be allowed

In chronic diarrhoea the treatment will vary according to the cause, the chronicity of the condition, and the presence of complications It is not proposed to go into this in detail but one may mention that drug treatment for diarrhoea is rarely satisfactory It is not wise to check the diarrhoea with opium, toxic absorption will increase and the patient will only feel much worse It is not wise to dose the patient with a variety of so called intestinal antiseptics We know of none which is effective It is not wise to overtreat the patient for amoebiasis or worms It is possible to poison him with emetine, bismuth emetine iodide or stovarsol If dilute hydrochloric acid does not work in three or four days, there is no point in keeping it on for months If given for a long time, it should be given through a straw.

In most cases the chief essential is to find a suitable diet A well balanced non-residue diet is the ideal In most cases it is best at the beginning to confine to two or three articles of diet which are well tolerated by the patient Milk, buttermilk, curds, and in fruits over-ripe bananas, mangoes, stewed apples or apple juice, and pomegranate juice are well tolerated by most patients On milk or buttermilk and banana or mango diet the author has treated numerous cases most successfully Patience and perseverance and insistence on a high calorie intake are necessary Where there is macrocytic anaemia liver extract by injections or liver and stomach extract by mouth should be given In the presence of avitaminosis, large amounts of all vitamins, and especially vitamin B, and Nicotinic acid are required Calcium and iron are needed in most cases Diarrhoea which is not checked by dietetic regulation will require kaolin, bismuth, or small doses of opium Isapgul and baelfruit are also useful in helping the intestinal mucosa to recover Active checking of diarrhoea with drugs is likely to produce much abdominal bloating and distress Colonic lavage with antiseptic drugs or with astringents is rarely of much use Silver, copper, mercury or tannic acid preparations are rarely used now-a-days Antistreptococcal serum or vaccines may prove of some value in some cases of chronic ulcerative colitis Sulfaguanidine or sulfadiazine may help in some cases

Critical Notes and Abstracts

SULFADIAZINE

Sulfadiazine was mentioned in *The Indian Physician* before (See Vol I p 155, 449, and 490) The drug is now available in Bombay and it is desirable to know something more about it Sulfadiazine (Jour AMA Feb 28, 1942, p 730) is a—2-Sulfanilamidopyrimidine $C_{10}H_{10}N_4O_2S$ It is an effective chemotherapeutic agent in the treatment of experimental meningococcal infections, pneumococcal, haemolytic streptococcal, staphylococcal, Friedlander's bacillus, E Coli, Clostridium septicum and Clostridium Welchii infections in mice Clinically good therapeutic results have been reported in the treatment of pneumococcal pneumonia, both lobar and bronchial, and haemolytic streptococcal, meningococcal and Friedlander's bacillus infections, also staphylococcus infection, gonococcal infections and urinary infections due to E Coli, A aerogenes, and staphylococci

Sulfadiazine, given orally, is slowly absorbed from the gastrointestinal tract, its excretion is also slow, and it takes five or more days after the drug has been stopped before it is completely eliminated from the body The slow absorption and excretion makes it possible to obtain and maintain adequate therapeutic levels of sulfadiazine with more ease than with sulfapyridine or sulfathiazole The drug passes into pleural and abdominal fluids and into the spinal fluid in concentrations of one half to four fifths of that noted in the blood It penetrates the red blood cells easily

It has relatively low toxicity Nausea and vomiting so frequent with sulfapyridine are not common, dizziness is only occasional and mental disturbances are rare There is no acidosis or peripheral neuritis or anterior horn cell injury Fever and drug rashes are rare, 1-2% only Hepatitis has not been reported, leucopenia with granulocytopenia and haemolytic anaemia are rare Only one case of agranulocytosis is reported Some five cases of anuria have been reported (Ind Phys Vol I, p 490) It is advisable to give fluids freely and keep the urinary output upto 40 ounces or more per day It is noted that patients who are suffering from acute toxic reactions from other drugs in the sulfonamide series may be switched to sulfadiazine therapy without much chance that the existing toxic reaction will be prolonged or accentuated by sulfadiazine

Uniform standards of dosage have not as yet been agreed on by investigators who have used sulfadiazine It is important to establish adequate concentrations of the drug in the blood as soon as is possible after therapy has been initiated In adults with pneumococcal pneumonia a large initial oral dose is given and should be based

No contraindications seem to exist. No evidence of toxicity or damage has been observed so far. The Vitamin D Shock Therapy seems to be entirely harmless. The doses of 600,000 international units of vitamin D resulted without any exception in an unusually prompt cure of even severe rickets and tetany unimpaired by the presence of acute or chronic infection. In some older children higher doses may be required for better results. These doses are given by mouth, the most simple and effective way of administration. It should be incorporated in milk. Care should be taken that no active substance is lost by adhesion to the bottle or other receptacle. Vitamin D is effective and should be given in certain cases intramuscularly or subcutaneously. In private practice, in clinics when the child refuses milk or vomits, when the child has diarrhoea or Vitamin D is not utilized, Vitamin D Shock Therapy is given parenterally. Vitamin D administered in one massive dose is retained in the child, much more so in rachitic child. Most of it is stored in the skin, liver and brain. It can be given as a prophylactic treatment in infants. The most favourable time for the Vitamin D shock prophylaxis is at the end of November or the beginning of December when the Vitamin D reserve stored during summer and early autumn is about to be exhausted. This should be repeated in the second winter of life.

J C P

ALCOHOLIC GASTRITIS

Alcohol has been invoked as an aetiological factor in a number of conditions like cirrhosis of liver, cancer of stomach, alcoholic neuritis without adequate reason or further research has shown that it does not play any part in the aetiology. Dr L. H. Berry (J Amer Med Assoc 1941, 117 p 2233) examined 100 chronic alcoholics gastroscopically. Most of his patients had been drinking hard for 15 years or longer. Some were taking as much as 2 or 3 pints of whisky, others a gallon of beer daily, 90% were also heavy smokers, most of them had tremors and cramps and were often drunk. Among these 100 hardy addicts, 84 suffered no distress after meals. They took large quantities of condiments, such as pepper and horse radish, ate all kinds of meat, baked and fried food and had normal or slightly loose daily bowel actions. Their only digestive symptom was morning nausea and when present it was mostly relieved by the first drink—usually about half a pint of whisky in the morning. When these almost symptomless drinkers were gastroscoped, the gastric changes seen were strikingly less in evidence than those observed in non-alcoholic gastritis. In 35% the only changes noted were those corresponding to simple hyperaemia, which were regarded as a mild chronic superficial gastritis. In 17% changes were of a moderate degree. In 26% the mucosa appeared to be normal, the remainder having various stages of true atrophic or hypertrophic gastritis. Among these heavy and persistent drinkers symptoms

were negligible and gastric changes were slight. In 16 subjects who actually drank less alcohol than those 84 there was higher incidence of gastritis and some degree of digestive symptoms. Putting all these results together Berry concludes, that in 100 unquestioned cases of chronic alcoholism unequivocal chronic gastritis was present in only 35%. Normal gastric mucosa can also be present in chronic alcoholics.

J C P

EFFECT OF LIVER THERAPY ON ERYTHROPOIESIS

In an interesting article published in *Quarterly Journal of Medicine*, Vol. XI, 19 (1942), Davidson, Davis and Innes show the effect of liver therapy on Erythropoiesis as observed by serial sternal punctures in cases of Pernicious anaemia. There has been two theories of Erythropoiesis in the cases of Pernicious anaemia. One is that due to lack of antianaemia factor, there is arrest of development at the stage of megaloblast which when antianaemic principle is supplied develops into Erythroblast and further into normoblast. Other is that following liver therapy in a case of pernicious anaemia megaloblastic blood formation ceases, the remaining megaloblast developing rapidly into megalocytes which enter the peripheral circulation and that concomitantly a multiplication occurs of normoblasts previously present in small numbers resulting in the restoration of normal marrow picture. In their experiments they used anahaemin or reticulogen liver extracts in the doses of 4 cc and 2 cc respectively. They have done repeated sternal punctures first, before beginning of the treatment, second, few hours (6-32 hrs) after the treatment, third, after 3-10 days after the beginning of the treatment and differential counts of all nucleated cells were made, 400 to 500 cells usually being counted. In addition 400 cells of Erythroblastic series were counted. These cells were divided into 4 types of cells from the early megaloblast to late normoblast. The colour of cytoplasm, whether basophilic, polychromic, or orthochromic, arrangement of chromatin in nucleus and presence of mitosis in cell, were recorded. They have shown in tables and in graphs that earliest change in cytology of nucleated red cell occurs within 6 to 10 hours of the initial injection of liver extract. This change consists of a reduction in the mean size of predominant cell type accompanied by a striking change in the character of the nucleus. After 32 to 72 hours the change is still more pronounced and in conventional terminology, the megaloblastic picture becomes normoblastic. No significant increase in mitotic figures were seen from these results. The authors conclude that under the influence of liver therapy megaloblast develops directly into normoblast from which it develops into normal red cell. They believe that megaloblast and normoblast belong to one development series.

J C P

MYOCARDIAL INFARCTION

H W Rathe reviews clinical features and prognosis of a group of 274 cases of myocardial infarction seen during or shortly after what was considered to be the first attack (JAMA Sept 12, 1942, Vol 120, No 2 p 99). Of these 274 cases 20% (55) formed the first early fatal group 50% (135) formed the second or late fatal group, and 30% (81) formed the third or survival group. The sex ratio of men to women in the series was 2.4 : 1. The average age of the entire group was 59 years. The age of the early fatal group was three years older than that of the survival group. The persons in rural areas were frequently affected and in all probability occupation in itself was of little significance in the etiology of coronary disease. History of hypertension and a family history of cardiovascular disease was significant. Of the possible exciting factors, unusual exertion and excitement were noted in only about 12% of the cases. The symptoms associated with the infarction were "Preliminary pain," severe pain, moderate pain, paroxysmal dyspnoea, fatigue-apprehension and acute pulmonary oedema. Of the clinical signs heart rate over 100, shock, muffled sounds gallop rhythm, friction rub, subsequent cardiac enlargement and congestive failure were studied from the diagnostic and prognostic view point. A poor prognosis was indicated when (1) a sinus tachycardia of 100 persisted over five days, (2) the age of the patient was over 55 years, (3) the systolic blood pressure dropped suddenly and failed to rise again to a level of 100 mm of mercury within five days, (4) unusual fatigue and apprehensiveness were prominent during the early convalescent period, (5) congestive failure developed, (6) the pulse pressure was 20 mm, of mercury or less, (7) the electrocardiogram revealed an anterior infarction or an indeterminate infarction, (8) there was a gallop rhythm present.

A good prognosis was indicated where the above factors were not predominant. This was especially true if (1) the patient was under 55, (2) the heart rate did not reach 100 or if it dropped within two or three days to 90 or less, (3) the blood pressure returned to a near normal level, (4) the heart was not enlarged, (5) there were no signs of cardiac failure. The patient with these good prognostic signs should live many years if carefully managed.

Announcement

We are requested by Burroughs Wellcome & Co, London, to make the following announcement to our readers —

THE WELLCOME MEDICAL DIARY, 1943

Difficulties of production, transport and distribution have made it necessary to discontinue the Wellcome Medical Diary during the present emergency. The publishers regret profoundly the inconvenience this may cause medical men and hope that it may not be long before the Diary can once again be distributed in India.

The Indian Physician

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BOMBAY 2

to cure and the most fatal" Sea voyages and rest were prescribed The credit of stressing contagion of phthisis goes to Aristotle (384-322 B C) But Hebrews appear to have been the first to proscribe the eating of the flesh of Tubercular animals

Till the period of renaissance, there was blind obedience to ancient medical authorities as perpetuated in Galen's (131-201) writings Galen believed the nodules or tubercles of the lung to be due to coagulation of vitiated body humors He advised against mixing with the consumptive patients The Arabian Physicians, Rhazes (850-923) and Avicenna (980-1037), likened ulcers of the lungs to those of the extremities and were pessimistic about the cure though they recommended the virtues of dry air and fresh milk Tuberculosis remained a hopeless and mysterious puzzle Due to the ignorance of pathological anatomy no advance could be made, dissection was not allowed

In the 14th century the practice of "Touching for the King's Evil" started in France and Queen Elizabeth and Charles II both exercised their royal prerogatives Rabelius (1490-1533) wrote satirically about this practice but till the writing of De Fabrica and beginning of modern anatomy by Andreas Vesalis (1514-64), no real advance was made or could be made In 1546 Fracastorius published "De Contagione" wherein he states that invisible germs carry the contagion of phthisis and these germs arise from within due to putrefaction of the humor as well as from without He advised the inhalation of a red o pigment, sulphide of arsenic, for destroying the germs Fracastorius stressed the need to "combat germs and prevent contagion"

The idea of contagion, specially through sputum, was specifically propagated by Micheal Ethmuller (1644-1683) of Leipzig, and Italy was the first country to pass the preventive legislation The great poet Keats was forced to have his supplies through a window in Rome where he died of Tuberculosis

As early as in 1638, Robert Fludd suggested injection of sputum in treating tuberculosis Outstanding contribution to the study of the disease was made by Franciscus Sylvius, the anatomist of Leyden (1614-72), though a firm believer in Hippocratic humoral pathology He stated that tubercles were often seen in the lungs in cases of consumption and that they would sometimes soften, suppurate and form vomicae He thought

that Tubercles were enlarged glands and he did not differentiate them from ulcers. It was Thomas Willis (1621-75), who studying the anatomy of the lung nodules stated that phthisis could exist without actual ulceration of the lungs. The first serious English contribution came from Richard Morton (1637-98) by his treatise entitled *Phthisiologia*. He states that phthisis "is accompanied by fever and springs from a defective state of the lungs and from the resulting ulceration of pulmonary tissue". He advocated Cinchona bark for haemoptysis. In 1733 Pierre Disault published an able dissertation on the morbid anatomy of the tubercles and believed that sputum was the means of propagation of phthisis. William Stark (1740-1770) of Birmingham was the first to distinguish between Tuberculosis and Scrofula and made a detailed study of the anatomy of tuberculous lung. He stated that tubercles were not enlarged lymph glands but local neoplasms. He also wrote about adhesions in the lungs. Gaspard Laurent Bayle (1774-1816) was the first to employ the term Tuberculosis. He pointed out the nature of scrofulous glands and described the relation between pulmonary tuberculosis and tuberculosis of other organs. He did not believe that haemoptysis caused phthisis. In 1793 the publication of morbid anatomy by Mathew Baillie systematised pathology.

In the year 1815 when the battle of Waterloo was fought, Laennec invented stethoscope and brought order out of chaos in clinical medicine. He established the specificity and unity of the tubercle and recognised the latency of the disease. He clearly described the developmental stages of tubercles from great tubercles to caseation. He stated that tuberculosis can heal after evacuation of caseous material by fibrous transformation.

The importance of an evening rise of temperature as a criterion of the severity of the disease was first pointed out by Thomas Young (1773-1829). In 1837 William Stokes wrote "Diseases of the Chest". He noted reflex muscular excitability of chest muscles in pulmonary disease. In 1839 Schwann's paper on the cell theory appeared, and Joseph Skoda systematised the technique of Auscultation and Percussion according to the laws of sound.

Rudolf Virchow (1821-1902), the founder of Cellular Pathology, claimed that the inflammation in phthisis might terminate

in caseation, the tubercle is a non-vascular granuloma, the result of local cellular proliferation. With his publication of "*Cellular Pathologie*" in 1858, the ancient humoral conception of tubercle formation is finally forgotten.

In 1843 Klencke showed that Cow's milk could transmit tuberculosis. Though he is also claimed to have produced Tuberculosis in rabbits' viscera, real credit is given to Jean Antoine Villemin (1827-1892) French military surgeon, who demonstrated that human pulmonary tubercle could be inoculated into rabbits and showed clearly that tuberculosis was a specific infection. He thought that phthisis was an exclusively contagious disease. He really described the tubercle best and by observing that tubercles occurred in other parts of the body than the lungs, concluded that tuberculosis was not a disease of the lung only.

The dangers of pulverised dust that had become infected with dried tuberculosis material, e.g., sputum, was pointed out in 1869 by Chauveau as well as by Villemin and Cornet (1890), whilst Flugge pointed out the danger arising from "droplet infection" from mouth, nose, etc.

The microscopic work and intensive study in Bacteriology that began with Leuwenhoek, furthered by Pasteur's proofs for the denial of spontaneous generation, found climax in Robert Koch's identification of the tubercle bacillus. Koch found that tuberculous animals resist re-inoculation. He introduced tuberculin and his work has become the guiding spirit to all subsequent investigations.

The production of immunity is carried out by two ways, first by the original method of Koch and the other the way of Sir Almroth Wright, by the use of small doses at long intervals. In 1917 Owen Paget advocated inhalations of the patients own dried sputum at first, and then of bacillary emulsion insufflated through a glass tube. In 1924 Weill-Halle and Turpin began in earnest vaccinating "children by mouth with what they called B.C.G.—i.e., a race of tubercle bacillus obtained after 13 years and 230 cultures that have lost their former property of producing lesions of tuberculosis. But the new race has retained the property of producing tuberculin and of calling forth the formation in the organism of antibodies." In 1933 Calmette showed

that the immunity conferred by B C G lasts more than five years and that revaccinations are harmless

Yet the struggle against tuberculosis is not over The world is anxiously awaiting the birth of an Ehrlich or a Dogmack to produce a chemotherapeutic agent against tuberculosis bacilli In the meantime the commonest practice is change of air at higher altitude, sea voyages and pinewood, the so-called "Shibboleths of tuberculosis" as Marcus Paterson (1870-1932) suggested Hippocrates, Pliny and the 17th and 18 century physicians advised horse-riding which took the patient out in the open air But it was Brehmer who seriously advocated what may be called "Open-air Treatment" and in England the credit goes to George Boddington In 1840 in his treatise Boddington taught, "the application of cold pure air to the interior surface of the lungs is the most powerful sedative that can be applied and does more to promote the healing and closing of cavities and ulcers of the lungs than any other means that can be employed" Though his views were very unkindly criticised in *Lancet*, as very crude ideas, even today the open-air treatment is the sheet anchor of the physician, inspite of the revolutionization of the treatment and diagnosis by the invention of x-rays by Roentgen in 1895 and the use of Pneumothorax and other surgical measures The first sanatorium opened in India was in 1909 at Dharampur near Kasauli Except for two or three missionary efforts, and a few private ventures, one can say that India has not adapted the sanatorium line of attacking tuberculosis as she should have

Gold has been used by Hindu physicians in the form of "Suvarna Vasant Malti" since the ancient days but in the west Paracelsus first used its bichloride salt prepared by Christien in 1810 The present popular salt, Sanocysin, was introduced in 1923 by Holger Moellgaard, a Danish physician Another popular therapy viz, Calcium therapy, was introduced by Renon in 1906 as he observed that workers in lime burning furnaces never suffered from tuberculosis Ancient Indians and the present day practitioners of Ayurveda use praval and pearls freely, which is nothing but calcium Looft and Blum had noted in 1901 that the calcium content in the blood was found to be diminished in tuberculosis and Emile Sergent advocated the recalcification of the decalcified organism Philip Ellman in 1924 could not confirm the supposed diminution of the calcium content of the blood in pulmonary tuberculosis Yet calcium injections alone

or with Parathyroid or Vitamin D form the routine treatment at present

Nascent iodine was once in fashion, introduced by Pfannenstill in 1912, so also copper salts in France and Germany Percy Mosey in 1927 introduced colloidal antimony by intramuscular injection Garlic the popular remedy with the Hindus since the time of Charak, was used by Vivian Poore in 1894, and earnestly advocated by W E Minchin and John Knott (1904) of Dublin Cod liver Oil has been widely recommended since first used by Percival in 1774 In 1909 it was shown by C T Williams and Forsyth that *in vitro* Cod-liver oil inhibited the growth of tubercle bacilli—the fact confirmed by Campbell and Kieffer in 1922 Preparations more concentrated in vitamin contents like halibut oils are popular In India, the oils of Ghos and Ravas fish, highly rich in vitamin A, were introduced under the name *Adol*

Here only a mention will be made of collapse therapy, thoracic surgery and helio-therapy In 1803 Itard was first to apply the term pneumothorax denoting gas in the pleura But James Carson in 1821 seriously advocated the collapse therapy and in 1832 F H Ramadage is stated to have punctured the chest wall But it was as late as 1906 when Carlo Forlanini published the report of his 36 cases that the collapse therapy started becoming popular In 1912 and 1913 Maurizio Ascoli and Parry Morgan performed bilateral pneumothorax The invention of the thoracoscope by Jacobaeus of Stockholm in 1912, greatly facilitated the practice of pneumothorax In 1911 Erns Stuertzt suggested the idea of paralysing the diaphragm by the division of the phrenic nerve on the affected side, and in 1936 Laurence O'Shaughnessy suggested "phrenicoplasty" in place of phrenic crush as it was found advisable to produce a temporary paralysis by crushing the nerves instead of dividing it or tearing it out

Estander in 1879 introduced the word thoracoplasty In 1890 Carl Spengler introduced the extrapleural thoracoplasty and Sauerbruch in 1909 used extrapleural posterior thoracoplasty

Yet neither the physician nor the surgeon can claim that he has conquered tuberculosis and the human enemy No 1 takes regularly a heavy toll, particularly in the ill nourished inhabitants of India

Original Contributions

WHAT IS TUBERCULOSIS?

By

R. B. BILLIMORIA

M. D. (BOYD)

BOMBAY

Thus once wrote Allen Krause "Predisposition, substandard constitution, fresh air, milk and eggs, universal tuberculosis, incipient diagnosis, signs in the chest (of what, pray), nutrition!" Isn't it about time to make all these fellows toe the mark and *prove* exactly what they mean by such juicy mouthfuls? Let's make 'em answer 'what is tuberculosis?' You will get a hundred damful views *What causes tuberculosis?* All the fresh air in the world won't have the least effect of *itself* on tuberculosis so long as strain is kept up—*Only don't stop studying tuberculosis*—by using every talent and every ounce of energy you possess to straighten out the tuberculosis problem and put it on a sane foundation"

There are various methods of approach to the study of a disease historical, anthropological, statistical, epidemiological, experimental, immunological, pathological, clinical, therapeutical, etc. Individual study of one or another of these never can help, but even the aggregate leaves us far behind till we study a particular healthy vs a diseased human body, his *nature* his *individuality* (not only as regards his environment but as pertains to his very germ plasma since it was impregnated carrying ages old hereditary taints), his tissues, body fluids, viscera, the interconnections and the balance and the imbalance between these and the so-called ductless glands, his psyche, his ego, his everything that happened to him from impregnation, from birth to death

There is no cure for birth or death. What we want is to enjoy the interval. And tuberculosis has marred this interval in millions. But going on and on with the age-old ideas, slavish acceptance of opinions through respect for antiquity and so-called authority, have till now led us to no where. The tuberculosis

campaign that has been waged till now is not in the least a conquest. If with all the great efforts of America (where thousands of beds are set aside to treat tuberculosis, that nation has to mention 61,000 deaths in a year) we can safely say that a person becomes tuberculous, cures himself or kills himself on his own

"Prove all things, hold fast that which is good" (Epistle to the Thessalonians). Tradition and authority have always figured largely in medical conceptions, and practice, experience and obvious facts have often been ignored—even intentionally, when such seemed not to confirm with orthodox teaching. Statements are accepted as gospel truths on the magic of a great name, and made to represent a truth by constant repetition on the lines of Hitler's maxim that oft repeated lies are finally taken as truths.

"Every fool believes what his teachers tell him, and calls his credulity science as confidently as his father called it divine revelation." A medical student has, what one might call, blotting-paper tendencies for picking up impressions and ideas from his teachers, who to him at that period of his life are like demi-gods. And these impressions are too difficult to be wiped off in his future career and progress. The advice of Oliver Wendell Holmes is "we must not only take a good stand, but keep progressing," but unfortunately, in the disease tuberculosis we have not even taken a good correct stand.

I remember the story of a great Greek philosopher, who daily went to a museum and attempted to discuss his theories with dumb statues. When he was asked the reason of this queer behaviour he answered that he was preparing to give out his theories to the world where he did not expect any better hearers than these marble statues. But the fate of one, who wants to say something against the established views in the science of medicine is worse still. Rebuffs, derision, insults are his reward. I may repeat here the story of George Boddington who advocated as far back as 1840 the open-air treatment of "Pulmonary Consumption" the importance of a generous diet, fresh air day and night, together with systematic arrangements with regard to exercise and general treatment and the watchfulness daily—nay hourly—over a patient of a medical superintendent." Boddington met with the most bitter and contemptuous treatment from the public, and even by the Editor of the journal *Lancet*. He was

regarded as a lunatic and by the irony of fate, he was compelled to turn his sanatorium into an asylum for the insane

The culprits, if one might call them so, who have hampered the study of the disease tuberculosis are the bacteriologists and the T B specialists.

Laboratory experiments are taken as imitating—mimicking—human diseases, but which, in fact, are worse than gross caricatures. The study of the science of bacteriology is something like riding a donkey. In some diseases, such as diphtheria, it has made a lord of the rider (the bacteriologist), but in the disease tuberculosis it has made a groom a blind slave of him. "We are more and more being convinced that phthisiogenesis is more a problem of predisposition than of bacterial infection" (Fishberg)

The general practitioner sees his patient through many diseases from his childhood—why rather from his very proto-plasmic stage when he was as such in the womb of his mother—in the course of which he acquires knowledge of the relationship of heredity, environment, coincidences, exciting (probable) factors, constitutional types to diseases, of one disease to another the different temperaments, moods and what not. A consultant only comes late like a boot-repairer to put on a new sole on an old mis-made boot, which now gives way at some other spot (formation of new foci of disease in other part of the body). But the poor unfortunate family physician, with all the unproved stuff given him in his student days, has his capacities of stretching his imagination and thinking qualities blunted. Any idea from him is pooh-poohed by the great consultant whose only concern, as Osler said, was to do the talking and pocketing the fees. Tuberculosis can be accurately and correctly studied not in a tuberculosis sanatorium, but outside it, in general public life,—in the country, in the town, in a hut, in a palace, amongst the starving and the rich, amongst the healthy and the weaklings amongst people of all ages with complications of other diseases or not. In this way alone can be studied the various reactions and responses of a tuberculous case living in its natural surroundings often fairly, at times quite successfully fighting out the disease in spite of all the factors described by the Tyneside enquiry as favouring the onset and spread of the disease.

Just let us consider the oft repeated complaint of the great specialist,—that the disease has been diagnosed very late by the

family-physician Can we not ask in turn, what he *means by an early diagnosis* In the first place, isn't it high time one, once for all, discards the term Pulmonary Tuberculosis, and replaces it by a correct scientific name "*Tuberculosis, with predominant symptoms in the Lungs*" Now our young future medicos begins to realise the full meaning of the term pulmonary tuberculosis But the specialist does not himself know what he wants to imply by early diagnosis He classifies his lung trouble into three stages I-II-III on the *anatomical extent* of the disease Is there any disease where anatomical classification is at all applicable except in traumatic surgical injury, where too, more often than not, there are many other complicating factors which would not permit of such a classification? The very term "early" is indicative of one's gross ignorance of the pathology of the disease It can only be applicable to the earliest days when the patient came in contact with an *open* case of tuberculosis, and had his first dose of the bacilli But even then one could never venture to give a prognosis, nothing may turn out of it, or the baby may die of tuberculous meningitis or miliary tuberculosis

The "incipient" or early stage does not invariably mean a curable condition of the disease, as what looks as an advanced condition as surmised from an X-ray picture and physical signs does not necessarily indicate a hopeless outlook, such patients (the Productive type and several of the Proliferative type), being known to have lived decades in spite of their sputum showing T.B. An *acute exudative phase* with high temperature and pulse rate with sputum laden with T.B., in a productive type of lesion, subsides within a few days giving credit to some new-fangled treatment whilst a *massive benign pneumonic* type leaves not even a trace behind, although the onset was so stormy If the specialist wants the family physician to diagnose the case early, will he accept these as early, though his principle of anatomical classification puts them in the III stage? If the unfortunate family physician takes this advice and calls it III stage, the patient leaves him, goes to a Hakim or a Vaid or a Homoeopath, or still more likely buys some very costly patent drug with a high sounding name and gets cured and advertisements thereon appear in lay papers

Another thing which keeps a specialist busy is his very favourite theme "*Tuberculosis Surveys*" Why he does that he never answers Once he says that in all towns and cities 90%

of the population is infected with T B Again he says this primary infection of childhood is a sort of protective inoculation, and he goes further and wants all babies to be inoculated with B C G and keep on inoculating till they react positively to his tuberculin But at the same time he raises a hue and cry if his tuberculosis survey shows a high percentage of positives in some district He has never till today thus told us definitely whether it is good or bad for an individual to have a positive tuberculin test

Then he argues that long—i e, by centuries—contact with the tubercle bacillus gives a sort of immunity to a race And in support quotes the high mortality rate amongst the negroes in America, where the disease was brought fresh from the civilised world in this so-called virgin soil But then this statement received such a rebuff from Col Bushnell¹ "There can be no question that before the Civil War the Negro was in the same condition as respects infection with tuberculosis as the whites, in other words he was tuberculized practically to the same degree as his master, the almost identical mortality rate in the two races proves this beyond question The frightful mortality after emancipation must, therefore, be explained on other grounds than that of primary infection of a completely non-immunized population" And one more rebuff China with its tuberculosis of 2000 years and more has the largest mortality, in spite of this long tuberculation

One does see the value and importance of Tuberculosis Surveys One can thus find in a family an open case But what are we now going to do? Have we got laws and facilities to isolate this open case? Cannot then one say that unless these surveys are followed up by isolating all open cases, it is all a wasteful effort? And even then again further we have the advice of the late Allen Krause² "Perhaps our most important practical task is, for the time being at least, to accept infection as part and parcel of the normal make up of man, and lay emphasis on preventing morbidity" Vajda, from a study of 683 married couples concludes that "as regards exogenic reinfection great importance must be ascribed to disposition, the immuno-biologic conditions of the individual, and all factors which influence these conditions favourably or unfavourably" "Because of the ubiquity of the tubercle bacilli there is hardly a person living in a large modern city who has escaped infection In other words,

despite the vigorous and costly campaign which has been made during the last fifty years, the majority of the population in civilised countries harbour tubercle bacilli" (Fishberg³).

To put it in simple terms,—in the disease *tuberculosis*, infection, morbidity and mortality are three quite different things, one does not depend on the other. The study of this disease mainly and solely from the standpoint of bacteria, the tubercle bacillus, reminds one of a drunken man—a reveller, who catches the lamppost more to support him (his bacterial theory), than to use the lamp above him as the guiding light.

Isn't it strange that in the five criteria given by that master diagnostician Lawrason Brown, in the diagnosis of tuberculosis, there is no mention of this tuberculin test? Now after years of this wasteful energy on tuberculosis surveys, the National Association for the Prevention of Tuberculosis⁴ discards this as of no practical utility.

Now let us consider the aetiology of Tuberculosis (besides the presence of the Tubercle Bacillus) that is given to us by our masters. The Tyneside Enquiry gave us over-crowding, poverty (starvation), insanitary living (want of air and light), and pregnancies as the exciting causes of the disease.

Let us consider *over-crowding*. It was shown at the last Belfast Conference, giving instances of Chile and other places that the population ratio area of land did not prove the contention. Further it was shown that industrialization, meaning thereby big towns which naturally means over-crowding, reduces mortality rate from tuberculosis.

Chile has a population of 15 per square mile with tuberculosis mortality of 245 per 100,000, New Zealand only 45 with the same population, Denmark 163 with a population of 224 per square mile.

Air and ventilation the Tubercle Bacillus is almost an obligatory aerobe, by collapse therapy we deprive the focus of disease of free circulation of the oxygen-carrying blood, mountain climate which has definite beneficial effect is poorer in oxygen than air at sea level, during shallow breathing only one seventh of the air contents of the lungs are renewed, and still less during the absolute bed rest that we enjoin in the treatment, bed rest further tends to produce disuse atelectasis of the basis and marginal areas, it is a strange fact that coal-miners⁵ suffer

far less from tuberculosis, (they are even taken to be immune to tuberculosis) working in the dark coal pits with very poor air conditions than their own relatives on the surface of the earth

Consider further a case of acute rheumatism going on for three months and more, kept as it is on very low diet particularly as regards its protein contents, covered up with blankets and all sorts of fomentations, with its characteristic anaemia. Although his tuberculin tests be positive, as I have often done these out of curiosity, these cases have never in my records developed tuberculosis, though some of them have passed these months of imprisonment almost three, four and more times. Why, in fact, it has been definitely noticed that acute rheumatic fever in a good thing for a consumptive, just as an acute attack of jaundice is good for rheumatoid condition.

And still we are told the prime cause of tuberculosis is insufficient ventilation, and we are asked to advise our patients to keep open windows day and night, and sleep in open porches. Workers in Silica who get more air and light than coal-miners are most prone to tuberculosis. Pickof even has devised a very interesting modification of the guinea-pig inoculation test: he mixes silica with the suspicious material for injection to give quicker and more accurate results. Is it then the darkness and air-deficiency or something else which favours tuberculosis? To repeat Krause's word "all the fresh air in the world won't have of itself the least effect on tuberculosis."

Privation and insufficient food. We are taught tuberculosis is a germ disease, and starvation and privation is now said to increase its activity and virulence. Against this we are told by Laidlaw and Macfarlane⁶ that the increase in tuberculosis in Glasgow was due to long hours of work, general strain and ill-spent leisure. Under nourishment was named as one minor factor. Long gives an excellent survey of the food problems and severe food shortages in various countries during war times, and states "that malnutrition is rife in certain portions of the continent is perfectly clear. Whether or not it is accompanied by a rise in the tuberculosis rates is not yet evident." But the bomb-shell comes when one reads about the researches of Rivers, and of Reed. Nearly three decades back Rous⁷ showed that under-nourished fowl are relatively immune to sarcoma virus. Recently, Rivers in his work on Infantile Paralysis founded the theory that

I would say that Tuberculosis is a "*Conditioned Infection*" In other words, a man is harbouring some factor in him which enables the latent—or a fresh tuberculous infection to develop into a disease Whether this be some biochemical change in his tissues, some deficiency or excess of an hitherto uninvestigated substance, presence of some other infecting organism or what not time may settle In proof of this contention I may site the following

1 So many mouths harbour fusiform bacilli spirillae, amoebae, etc Why is it that these become more active in scurvy—deficiency of C vitamin, and in agranulocytosis?

2 Roholm and Kraup⁹ have shown that so called arsphenamin jaundice is really an epidemic jaundice (hepatitis) The arsphenamin damages the liver, and prepares the way for the hitherto unknown virus of epidemic hepatitis, latent in the body

3 In swine-influenza¹⁰, symbiosis with a virus is essential, without which the swine-influenza bacillus produces no disease, same way the virus alone is incapable without the presence of the influenza bacillus

4 Sanarelli sounded a new theory of infection in Typhoid fever fifty years ago "that E Typhosus was a non-pathogenic mechanical carrier of some unknown anti-catalytic toxic enzyme" Felix²¹ took up the matter, and started the question of Vi antigen, and Friedberger brought forward proofs that the disease typhoid fever was a double "entity", the E Bacillus and an ultra-virus The Italian worker Magrassi's work with brain extracts has unfortunately come to a halt, at least to our knowledge But this shows the synergic theory has come to stay even in the disease Typhoid Fever

5 A certain bacillary infection in rats remains latent without showing in the least any symptoms, though the blood shows the organisms But after splenectomy, the animal dies with symptoms of virulent septicaemia

6 Tuberculosis in a diabetic is in some mysterious way a peculiarly symptomless disease for a long time On the other hand in an alcoholic the reverse is the thing Acute rheumatism and nephrosis have a deterrent effect on the progress of tuberculosis

7 The extreme variations, according to the age incidence in man in the virulence of the disease are too well

septicaemic type in an infant, the slow healing one in childhood upto adolescence, the caseo-ulcerative and the caseo-pneumonic types in the age group between 16-30, the proliferative type after that, and again a virulent one after the age of 60

8 Different types of responses by different laboratory animals Compared with the guinea pig, experimental inoculation in the mouse elicits¹¹ a peculiar reaction The bacilli, originally basophilic, become eosinophilic rods and granules with reduced viability No caseation, no tubercle formation takes place Can one argue that a patient with the *productive* type of tuberculosis has in him some similar type of responsive capacity as the mouse?

9 The classification¹² as given by Ornstein, Ulmar and Dittler gives us the most accurate physiopathological idea about the disease seen in man (pulmonary tuberculosis), enabling us further in formulating a prognosis, as compared to our usual unscientific division into stages I-II-III Can we not ask why it is that different individuals react thus differently with entirely different pathological variations and different end results Shall we not make an effort to find out in health and in the infected state to find out by some method the type of response that will be there in a particular case

10 Similarly, in cases of pure glandular type we find in some small glands which neither caseate nor liquify, and keep on—there for years with an occasional addition of a new gland, another type caseates, discharges and heals even without any sterile surgical dressings, whilst the more common type enlarges, liquifies, keeps on spreading to new foci in quick succession and other organs getting rapidly infected Why is it that these cases won't heal in spite of all aseptic surgical attention?

11 We talk now-a-days so much about avitaminosis Yet even here we have some showing symptoms quite easily, and others like cases described in the *Lancet* (13-7-40, 49) can go on with impunity on absolute Vit C free diet for 100 and 160 days

12 We have in our teaching of pathology of tuberculosis the terms caseation, fibrosis, calcification, exudation In the first place we know not a word how these various phenomena take place, where and how these caseation and fibrosis, etc, come from We are told caseation is bad, fibrosis is good But why should it

be so in one and not in the other. Cannot one say that all these are responses as such, nature never meant them to be good or bad, but that they were pure responses by the conditioned condition of the patient to the same infecting organism, a peculiarity of that particular patient's tissue response?

By persisting on following our present line of methods in the study of this disease we will never reach the goal, more and more, mirage like, it will ever recede in proportion as we persist in our present theories. Little is known, much is written, and too much is discussed, and volumes exist by now to explain this unexplained disease. And this is through accepting unproved assumptions as basic facts, and building upon the insecure foundations a maze of fanciful conjectures. Graham Steel who died about a year ago, lived through full 90 years of a very active and strenuous life at the Edinburgh Infirmary with his ward full of acute lung (and heart) cases, and worked without any holiday till 1911. He was declared tuberculous with positive sputum in the year 1887, and with only just a short period of rest he put in all the amount of work. I have a patient now 86 years old, who was declared consumptive in 1888, had his sputum examined in England, and after a short stay there is here in India for over 50 years. Someone has so sarcastically remarked that all the stuff that has been said about tuberculosis as a disease in man, tells as much lies and untruth as is possible to do in the English language. Just as our present day Indian affairs may be described as a "mess in the chromosomes of politics" the description of the aetiology of tuberculosis that we have is a mess in the chromosomes of pathology and bacteriology.

We are told that with our newer knowledge, we have, by surgical and other methods, reduced the mortality from this disease. But when we come to actual figures we find that the morbidity—mortality ratio is just the same as it was 20 years ago.¹³ Trudeau Sanatorium Report shows that the longevity of life is better in those who had no collapse therapy.

In his autobiography "In Search of Complication" Dr Savitsch is made to utter these memorable words "Doctors accept the laboratory as an oracle when all it was meant to be was a test-tube," and these words by the great research man Dr Sewall himself.

Ever since Ehrlich's 606, our minds are centred on chemotherapy—and *sterilisans magna* Promin is now expected to revolutionize the treatment of tuberculosis. But the fundamental point in chemo-therapeutics that is not fully grasped by the medical world is the fact that the drug has not so much (perhaps none at all) action on the infecting micro-organism as on the *tissues* in which they are multiplying, by making them less vulnerable, and perhaps as well from some as yet undefined response of the tissues or fluids in the vicinity preventing the multiplication and even perhaps causing the disintegration and death of the infecting germ.

Lord Moynihan was wont to remark that surgery had been made safe for the patient, and our task was now to make the patient safe for surgery. Can we not similarly say we need not think of drugs to kill the bugs in our patient, but think of ways that will prevent the bugs from harming our patients?

A study of the psychology of a tuberculous case will help us a lot in the treatment of the patient. "Hope itself is happiness, and its frustrations, however frequent, are yet less dreadful than its extinction." "Hope is the companion of power and the mother of success, for whoso hopes strongly has within him the gift of miracles." *Spies Phthisica*. Nature teaches us thus how to treat a consumptive. There is hypocholestermoemia¹⁵ in tuberculosis, and this low cholesterol content is said to be the cause of the *spies phthisica*. In the Tubercle Bacillus we have Vitamin K and riboflavine, nature's safeguards against haemorrhage and intestinal complications. Nature thus is indirectly kind to the victim, and who knows it is thus better for a patient to swallow his TB laden sputum, to disintegrate them and liberate these vitamins. And blood is poor in its prothrombin in acute tuberculosis.

One might say we have got the power to cure, but unfortunately we do not know *what* to cure in this disease. There is no art in which long experience—but not that locked up in a TB sanatorium—is more necessary before coming to a decision—as in the art of medicine. Till we gain that, one can summarise the treatment of this fell disease in four words (which stands as the best treatment today for yellow fever), in the words of Sinval Lins—"Don't kill your patients." The source of power in medicine is Faith. Let the patient live on *Hope*. We can do that if we once for ever abolish those abominable terms I-II-III stages

Which medical man has not been asked by the unfortunate patient or the relatives, when the diagnosis is declared "Doctor, is it 1st stage or 2nd stage?" Has he ever been put that question in any other disease?

A Soviet cancer specialist has shown that cancer can actually be caused by unhappiness, (and cf Duke of Aosta and acute tuberculosis), and many medical men believe that without worry at least half of the illness and disease would be prevented. On the other hand happiness and pleasure can bring a great deal of zest and enthusiasm, vigour and health—vim, vigour and vitality. A good scientist has so frankly said that "even an occasional excursion for a glass of beer or an evening with girls (or boys) at a picnic may be a good thing, for although the amount of alcohol consumed may be bad for the health, the benefit from a healthy fun and merriment is vastly greater." Compare with this the mental factor of a TB case treated in a sanatorium with fixed rules by the clock, of doing things, and lying down in bed looking up to the roof and counting rafters.

In the treatment of this disease we have done enough experiments with overfeeding and various salt-free and other dietetic fads, climate, cod-liver-oils and gold and other specifics (!), inhalations, injections, surgeon's knife. Shall we not now cry a halt and say "Don't treat the disease, but treat the patient?"

Treatment is the goal of all medical men's efforts. We cannot improve upon the words of Sancho Panza in *Don Quixote* "The beginning of health is to know the disease." In trying to know this disease tuberculosis, a problem till hitherto unsolved, one begins thinking

1 Can the disease *Pulmonary Tuberculosis* be due to a symbiosis (synergistic) of the tubercle bacillus with a virus, the presence of the latter exciting the latent focus (reactivation), endogenous infection), or getting active by a fresh dose (exogenous infection)—(cf *Swine Influenza*)

2 Can the latent focus be activated by biochemical changes in the fluids, tissues, organs of a patient due to trauma²³, physiological changes (coming into adolescence, parturition) not quite normal, but acting in some perverted or exaggerated way, or by mental strain agony, worry, etc, acting on the internal secretions upsetting their balance or hair pouring out of or upsetting the vago-sympathetic balance which may act perversely on metabolic

functions, enzymatic actions destruction of some vital vitamin-like factor (e.g., biotin).

3 Should we not study the hitherto neglected subject, why in one case we get acute exudative phenomena, in another caseation, a third with caseopneumonic phase with disintegration, another showing fibrosis, and some showing calcium deposits? An extensive biochemical study of the organs and body fluids and tissues in these different types of patients (and in different animals which react differently to artificial infection with tubercle bacilli) may enlighten us further. Inoculation results in mouse we have seen above. In rabbits¹⁶ we get a peculiar phenomena, we may call that of latency first phase—an infiltration of both lungs, in sixteen weeks all shadows clear out, second phase—after 8-9 months all animals die from tuberculosis. I have been working on different blood tests to differentiate these different pathological conditions. Weltman's test, and the various blood indices¹⁷ e.g., Medlor's, Houghton's, Von Bousdoff's, Barton's ought to set one thinking.

4 A study of the *Chemistry of the tubercle bacillus*¹⁸—its various components, protein, lipoids, polysaccharides, and the products formed not only in culture media, but as well in human and animal tissues need much work yet. Can this factor explain the different pathological types of Olnstein that we see in human beings? And if so, should we not try to find what makes the patient responsive in one case to one ingredient, in another to the other ingredient? We cannot then take the fibrotic and the calcified types as healing phases of the disease, but only as an active phase of the disease but of a type which cannot harm the patient much.

5 And with the final goal—treatment in attempting the chemo-therapeutic method we have to consider the likelihood of success only if we remember the fundamentals of the chemotherapy.

(a) Bacteria require nutrition. What is the most essential need of the tubercle bacillus we have discussed, viz., deprivation of oxygen. As regards 'food', requirements of the organism the various culture medias, their pH values, the changes produced in the media, effect on growth by variations in the optimal contents of the essentials of nutrition in the media have to be studied. This nutritional knowledge of the organism will lead us on to the next stage of,

(b) the action of the 'inhibitors', how they work, how they modify the chemical composition and morphological variabilities of the organism And the effect of,

(c) such modified organism has to be studied in various sensitive and non-sensitive animals by their response as compared to the usual cultures at their optimum value

(d) Biochemical analysis of the fluids and tissues of animals responding favourably to a treatment as compared to when they do not, can help us in evaluating the favourable changes and lead us to attempt and produce similar changes in our patients

(e) In experimenting¹⁹ with a drug, we follow the methods adopted in the study of the drugs of the sulphonamide group, e g, the enzymatic effect Various combinations of a useful drug may be formed to intensify the inhibitor action, and equally cautiously avoid the reversals which may accidentally be given along with the original drug For example might be mentioned the combination of nicotinic acid with a sulphonamide drug—is this combination an inhibitor or reverser?

In conclusion I may quote Fishberg "Succeeding in elucidating tuberculous infection, but failing to explain satisfactorily tuberculous disease, bacteriology is at present considered by many authors as inadequate to clear up completely the etiological problems of phthisis This is not only true of tuberculosis, but of nearly all other infectious diseases "Today we know that to have identified the microbic agent of any pathological process,' says Theobald Smith, 'is but the beginning of the solution of the immediate problem, and that it answers but one of a long series of questions' During recent years thoughtful minds in the medical world have therefore again directed their attention to other factors, exogenous and endogenous, which are instrumental in the production of pathological processes"

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Case Reports

BRONCHOGENIC CARCINOMA

By
J K MEHTA
M B B S
BOYB 11

P G, a male aged 32 years came to the K E M Hospital, Bombay under Dr N K Sahai, on 23-11-42 for cough with slight expectoration for six months and irregular fever of four months' duration. The expectoration was not foul smelling. The cough became progressively worse and he is now having cough with mucopurulent expectoration about 2-4 ozs per day. He gave a history that he had lost about 14 lbs of weight during his illness before he came to this hospital. He was afebrile from the day of admission, 23-11-42 till 14-12-42. After that he developed a rise of temperature which persists till 3-2-43, the day of this report. The temperature was intermittent going upto 101° to 102°F every day and coming down to normal. There was no rigor accompanying the fever.

There was no history of having swallowed any foreign body nor of haemoptysis.

General Examination On admission, the patient looked well-built and poorly nourished. There was marked clubbing of the fingers. There was no enlarged glands in the neck or axillae. There was no evidence of venous thrombosis anywhere. The weight of the patient was 86 lbs on admission. On 3-2-43 he weighed 79 lbs. A total loss of about 21 lbs since the illness began.

Respiratory System

On 23-11-42 The percussion note was impaired on the right side of the chest at the back with diminished breath sounds over that area. No foreign sounds.

Alimentary System

Teeth Pyorrhoeic, Liver and Spleen not palpable. Bowels Regular, Appetite Good. Circulatory and Nervous Systems were normal, blood-pressure 115/80 mm of mercury. White blood cells 15,000 per cmm. Polymorphs 52%, Lymphocytes 45%, Large monos 2%, Eosinophils 1%. Sputum repeatedly negative for T B.

27-11-42 *Screening and X-ray* A dense oblique shadow was seen on the right side close to the right border of heart and filling up the cardio-hepatic angle. Movements of the right cupola of the diaphragm were diminished on right side. Perihilar fibrosis in both lungs.

Diagnosis of (1) Unresolved pneumonia (2) Collapse of the Lung as a result of carcinoma of a foreign body was made. In the month of December he was screened again. The dense shadow was replaced by a diffuse, more extensive and more hazy shadow at the right base.

11-1-43 The signs in the lungs were more marked There was diminished movement of the lower part of the right side of chest Apex beat was in normal position T V F was diminished on the right base There was impaired note in the lower axillary and interscapular and infrascapular regions on the right side Elsewhere, there was a hyperresonant note Breath sounds were diminished over the dull area and occasional crepitations were heard Vocal resonance was diminished

Sputum Negative for T B White blood cells 28,000 per c mm Polymorphs 90%, Lymphocytes %, Large monos 1%, Eosinos nil

Bronchoscopy was done under local anaesthesia by Mr Homi Gandhi, F.R.C.S Mucopurulent discharge was seen from the terminal part of the dorsal bronchus Lipiodol was injected through the bronchoscope and an x-ray was taken (see fig) It shows complete obstruction of the bronchus Dense shadow that was seen in a previous skiagram was replaced by a more extensive hazy light shadow on the right side



3-2-43 General condition of the patient was the same except that he looked much more emaciated Red blood cells 3.5 millions, Hb 56%, C I 0.8

The diagnosis of Bronchogenic Carcinoma is made on the evidence of collapse of the lung, complete obstruction of the bronchus, loss of weight, and no history of having swallowed any foreign body nor any evidence of it. The muco-purulent discharge and fever must be due to a secondary bronchiectatic condition and sepsis associated with it. Still, the possibility of complete obstruction due to a foreign body could not be completely ruled out, a foreign body transparent to x-rays might have got in, the patient not being aware of it. But one must remember that

Skiagram of the chest of P C after injection of lipiodol showing an opacity at the right base and failure of lipiodol to enter the opacity the right descending bronchus terminating in a sharp point about 2½ inches beyond the bifurcation of the trachea the bronchoscopic examination, by vision or by aspiration did not show any evidence of a foreign body

(My thanks are due to the Dean K E V Hospital and Dr N K Sahar for allowing me to publish this case. This case is referred to by Dr N K Sahar in a discussion on Bronchogenic carcinoma in this issue p 65)

Society Proceedings

The 22nd meeting of the Seth G S Medical College Staff Society was held on Saturday the 9th January, 1943 at 2 p m (S T) in the K E M Hospital, Bombay Dr J P Padshah was in the chair Dr L Monteiro (Pathology Dept) read autopsy reports on three cases of

BRONCHOGENIC CARCINOMA

Three cases of Bronchogenic carcinoma coming to the autopsy room during the course of 1942 were presented In a series of about 4,500 autopsies in the K E M Hospital there had been 22 cases during 16 years, no cases having occurred prior to 1930 The increased incidence, the etiology and symptomatology were discussed

Case reports

The first case illustrates Pancoast's syndrome A male aged 45 years, a coolly by occupation was admitted for retention of urine for 10 days and inability to use the lower limbs for 3 months The symptoms had been gradual in onset starting with pain in back and numbness in the inferior extremities until the patient was confined to bed ten days prior to admission

There were no pulmonary signs or symptoms In addition to the paraplegia the patient developed pain in the region of the third rib, axilla and forearm on the right side The right pupil was contracted The cerebrospinal fluid was haemorrhagic A Kahn test of the blood was negative The patient expired seven days after admission

At the postmortem examination the upper lobe of the right lung was found to be the seat of the growth which had infiltrated into the adjoining pleura and the chest wall eroding into the first and second ribs and causing a pathological fracture Medially it involved the bodies of the 7th cervical and the upper three dorsal vertebrae with a fracture of the body of the 1st dorsal vertebra and softening of the spinal cord in this region The mass also extended upwards into the root of the neck involving the larger blood vessels and branches of the brachial plexus

Metastatic deposits were seen in the mediastinal lymph nodes which were markedly enlarged. The phrenic nerve was found to be embedded in these enlarged glands. There were no other metastases. There was no pleural effusion and no bronchiectasis in the lung. The urinary bladder showed an acute inflammatory condition of the mucosa. Microscopically the tumour showed the characters of spheroidal cell carcinoma.

The symptomatology and the postmortem findings were suggestive of a diagnosis of superior pulmonary sulcus tumour described by Pancoast who believed, however, that these tumours arose from the embryonic epithelial rests of the fifth pharyngeal pouch. This hypothesis has been contested by many and it is now believed that Pancoast's tumour has no individuality except the effects due to its position.

The second case was a male aged 58 years, retired from active service, admitted in a semiconscious condition of 6 days' duration. There was a history of headache for 4 months. The patient had been operated for cataract 4 months prior to admission.

On examination there was paresis of all the limbs, sluggish jerks, lower motor neurone affection of the 7th cranial nerve on the right side and the right pupil was dilated and reacting sluggishly to light. In the lungs a few rhonchi were heard. Blood pressure was 190/110 mm of mercury.

Investigations

C S F normal

Non-protein Nitrogen of blood 33.3 mgm/100 c.c.

Urine gave a yellow precipitate with Benedict's solution and also showed a large amount of acetone.

Blood sugar 222.2 mgm/100 c.c.

The patient was treated for diabetic coma, but expired 36 hours after admission without regaining consciousness.

At the postmortem examination a growth was seen at the hilum of the right lung with metastatic deposits in the hilar glands, pulmonary artery, the right supra-renal gland, the dura mater and many large deposits in the substance of the brain. There was a hypertrophy of the left ventricle and an arterios-

clerotic condition of the kidneys Microscopically the tumour showed the characters of a spheroidal cell carcinoma The hyperglycaemia and glycosuria were probably due to pressure in the hypothalamic region by the metastatic deposits or to a pre-existing diabetes The other nervous manifestations could also be explained by a large number of metastatic deposits in the brain

The third case was a male aged 55 years, no occupation, and was admitted for weakness of the left side of the body Thirteen days prior to admission the patient had been treated in this hospital for a haematoma of the left frontal region and subsequently discharged

On examination a left sided hemiplegia was found Six days after admission, the patient became unconscious, with pin point pupils not reacting to light, spasticity of all the limbs, brisk jerks and bilateral extensor planter response

There were no signs in the other systems Blood pressure was 150/100 mm of mercury CSF —Proteins and globulins slightly increased, sugar normal, 8 cells, lymphocytes, no micro-organisms present

The patient expired ten days after admission

At the postmortem examination a growth was seen in the lower part of the upper lobe of the left lung with involvement of the hilar glands The pleura was infiltrated but there was no pleural effusion

Metastatic deposits were present in the left suprarenal gland and in the right peduncle of the brain A small haemorrhage was seen in the left peduncle The heart was hypertrophied and the kidneys arterio-sclerotic

It is possible that the haematoma in the frontal region was the result of a fall caused by the cerebral metastases The subsequent haemorrhage, probably in a metastatic deposit in the other peduncle was predisposed by the hypertension which was incidental

In the three cases presented no clinical diagnosis was arrived at, all came with extrapulmonary symptoms and no physical signs in the chest, and none had metastatic deposits in the liver which is supposed to be a common site

DISCUSSION

Dr Pool (Tata Memorial Hospital) said that the symptoms of early malignant disease of the bronchus were only cough and persistent respiratory infection. All patients over 40, especially men, with these symptoms persistent over 3 weeks, required investigation to decide for or against bronchial carcinoma. X-ray films of two cases were presented by Dr Pool, (1) to emphasize amelioration after deep X-ray therapy, especially when the bronchus was blocked and (2) to emphasize need for bronchoscopic examination in every doubtful case.

Dr R G Ginde read the report of a case of carcinoma of Bronchus, under Dr R N Cooper. The patient a Muslim middle-aged male, sailor by occupation came to the K E M Hospital on 20-2-41 for pain in the right side of his chest of 8 months' duration. He had no cough and no fever.

The patient had a knock against a table on his ship and the pain started a few days later for which he was admitted in a hospital in Glasgow. There he was diagnosed as a case of Traumatic Haemothorax. His chest was aspirated and the patient discharged.

He was also admitted in this Hospital with the same provisional diagnosis. Clinically he had signs of pleural effusion on the right side with displacement of the mediastinum to the opposite side. The liver was palpable 2 fingers below the costal margin. Fluoroscopy of the chest showed evidence of fluid on the right side. The chest was aspirated on 22-2-41 and about one pint of sanious fluid removed, containing (naked eye) blood, culture sterile, no malignant cells seen. Sputum was negative for tubercule bacilli. The patient was X-rayed again which showed some fluid in the costophrenic sinus and a rarefied area in the sixth rib on the right side. Suspecting that it might be a case of Bronchial carcinoma further investigations were made. Bronchoscopy showed that the right bronchus ended abruptly. The openings of the right upper and middle bronchi were seen without any induration. Then a Bronchography was done which showed a definite filling defect. Right middle and lower bronchi were not visualized. In the mean time the patient developed a mass of glands in the right axilla which on biopsy showed evidence of secondary deposit from a squamous cell carcinoma.

Dr N. K. Sahiar said that the second case cited by Dr Monteiro was his and he was responsible for the diagnosis of diabetic coma. The patient was unconscious with 222.2 mg sugar per 100 cc blood, with sugar and acetone in the urine. He had been previously operated for cataract. The patient expired and he was surprised to learn the postmortem diagnosis of bronchogenic carcinoma.

Dr Sahiar gave an account of a case then in the wards. A man of 32 had been suffering from cough and had collapse of the right lower lobe. He had secondary bronchiectasis. There was fever and marked loss of weight. X-ray examination could not be done as the films were not available. The patient was too ill for bronchoscopy. **Dr Sahiar** said that he would be glad if any one present could throw light which would help in the diagnosis of such a case without the use of x-rays.

Dr. R. G. Dhayagude said that he only desired to emphasize a few points which had been mentioned in the paper read by Dr Monteiro, viz (1) Three cases in one year, (2) Absence of pulmonary symptoms, (3) Metastatic affection of the C N S in all the three cases and (4) Absence of metastatic deposits in the liver.

Dr R. N. Cooper referred to the history of Lung Surgery from the days of Stephen Paget in 1896 to modern times. Graham of St. Louis performed the first successful pneumonectomy. He compared the results of surgery with those of irradiation in the treatment of these cases. Graham recorded that only 12 per cent of cases were found to be operable. He had been able to give relief from recurrence for anything from three to eight years. A series of 250 cases treated at the Mayo Clinic was also referred to by **Dr Cooper**, 125 of these cases were treated with deep x-ray therapy. The relief resulting from this treatment is recorded to have lasted for periods ranging from one to twelve years. The normal expectation of life in untreated cases was about one year.

Dr N. D. Patel said that the carcinoma of bronchus was not uncommon in Bombay, and for want of figures one could not say whether the incidence was increasing or not. He had seen about five cases in private. He felt that x-rays and lipiodol were essential in diagnosing the cases and x-ray examination after

pneumo-thorax had also been found useful. The treatment at the moment was very unsatisfactory since the tumour did not react well to x-rays or radium. One wondered if much could be done by surgical measures for these tumors which show such tendency for early and widespread secondaries. Bronchoscopy was the best help that a surgeon could give in the diagnosis.

Dr J P Padshah remarked that carcinoma of the lung was not an uncommon condition in the wards of the Hospital, but the presenting syndrome was often misleading and the disease was not thought of. Owing to the frequency with which metastases occurred in the brain odd cerebral manifestations which could not be properly explained, should make the clinician keep this possibility in mind. This applied also to bronchiectasis and pulmonary abscess. Both glycosuria and ketonuria may be associated with cerebral lesions of rapid onset and conditions like subarachnoid haemorrhage were not infrequently wrongly diagnosed as diabetic coma.

Rational Therapeutics

HAEMOPTYSIS

Is it haemoptysis?

By haemoptysis one understands coughing up of free blood and not mere blood stained or blood-streaked or rusty sputum which occurs in a number of pulmonary conditions. If there is free blood one should decide if it comes from the upper respiratory tract or from the lungs. Haematemesis should not be mistaken for haemoptysis. In haemoptysis the blood is bright red, frothy alkaline and mixed with mucus or pus. The blood coming from the lungs or from the upper respiratory tract may have been swallowed and vomited afterwards in an altered state.

But one must remember that often many patients are not sure whether the blood was coughed up or vomited. In severe haemoptysis the blood may be dark and without any froth, and in severe haematemesis the colour may be bright red or dark, in moderate haematemesis the colour is dark, much alteration and admixture with stomach contents. The reaction is acid and there are "Coffee-grounds"—small dark brown altered particles of blood. From pulmonary cavities, dark plum coloured lumps are occasionally coughed up, these are alkaline in reaction and should not be mistaken for "Coffee-grounds". Sometimes when the patient has swallowed much blood after coughing it up, the difficulties of differential diagnosis increase. The coughed up matter should always be seen, patient's or relative's mere word is often misleading. Deliberate deception should be kept in mind. Here the blood produced is from the gums, and when the specimen is seen there is no difficulty in recognising it. Animal blood or some red pigment, e.g., that of betel leaf or kamkum should mislead no one.

What is the cause?

The commonest cause of haemoptysis is pulmonary tuberculosis. Bronchiectasis and mitral stenosis are the next most important causes. Bronchial carcinoma, pulmonary abscess, wounds

of the chest wall, leaking aortic aneurysm, cardiac failure, and haemorrhagic diseases are other causes of haemoptysis to keep in mind. The heart should always be examined to exclude mitral stenosis or endocarditis and a rapid general examination should always be made to exclude early right or left ventricular failure or haemorrhagic diseases. Other detailed examination, especially of the lungs, must be postponed till the haemorrhage is arrested.

The course

Haemorrhage from pulmonary vessels is self-limited. Loss of blood from the pulmonary circuit tends to reduce the pulmonary pressure, which is only one third of the systemic pressure and to arrest the bleeding. The pulmonary haemorrhage is rarely fatal except from choking by the aspirated blood. When a large vessel is ruptured, say an artery without any support in a large cavity with thick wall, or an aneurysm which has ruptured into a bronchus, nothing will stop the haemorrhage.

The indications for treatment are (1) combating initial shock or fainting and choking in severe haemorrhages, (2) allaying the fear and anxiety of the patient and the relatives, (3) prevention of aspiration of the blood in the pulmonary field, with resultant pneumonia or bronchopneumonia, (4) checking the haemorrhagic tendency, (5) prevention of recurrence, and (6) treating the cause.

The amount of haemorrhage

I *Blood streaked or blood-tinted sputum or slight haemorrhage*

This requires no special treatment except allaying the anxiety of the patient with a suitable sedative, and keeping the patient under observation.

II Moredate haemorrhage

The patient should be in bed till the bleeding has stopped. The posture should be adapted to prevent aspiration of blood into the opposite side. The trunk should be raised, and turned to the bleeding side, if it is known. A sedative should be given to allay the anxiety. All excitement or activity should be avoid-

of extensive fibrosis, adhesions and cavitation with thick walls, it is difficult to produce a desirable collapse. In such cases other operative measures, pneumolysis, phrenicectomy or thoracoplasty will have to be considered.

Blood Transfusion is necessary when the patient has lost a considerable amount of blood. 300 to 400 c.c. of compatible blood should be given slowly. In the absence of blood transfusion, the fluid loss should be made up by saline injections.

IV Profuse haemorrhage

Bleeding from a large vessel usually chokes the patient to death before the arrival of the physician. If the patient is alive and cyanosed, the back of the throat should be tickled or a suitable rapid emetic administered. This will cause vomiting and will clear the bronchi, and sometimes give sufficient time to institute other treatment.

V After care

Some patients show a tendency to recurrent attacks of haemorrhage. These should be protected against it by suitable treatment—rest, diet and therapeutic pneumothorax. Heat and exposure to sun should be avoided. Proper treatment of the primary disease should be started immediately. The patient and the relatives are more likely to co-operate now, if they were reluctant before. After haemorrhage, the patient is prone to develop bronchopneumonia or pneumonia, which should be prevented if possible by suitable chemotherapeutic drugs. In a patient who had tuberculosis a small haemorrhage is not necessarily a sign of renewed activity of the disease, but its recurrence should be an indication to keep the patient under observation. Pulse rate, temperature, sedimentation rate, blood count, weight, clinical examination and X-ray appearances should guide one in excluding the activity of the lesion. If these findings are negative blood-stained or streaked sputum can be ignored.

THE MEDICAL TREATMENT OF MENORRHAGIA

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Menorrhagia is an unduly profuse and prolonged blood loss at each menstrual period following complete ovulatory cycles. It may be due to either local gross organic disease in the pelvis or to purely functional disturbances resulting from hormonal imbalance or from some other systemic disease in the body. The organic lesions in the pelvis may be of the nature of Acute or Chronic Salpingo-oophoritis, Fibromyoma and Endometrioma of the uterus, Intra-uterine mucous or fibroid polyp, Tuberculous endometritis, chronic subinvolution and chronic metritis and displacements of the uterus. Occasionally it may be noted that one of the menstrual periods may be menorrhagic in type and in some instances may not even be preceded by any period of amenorrhoea. In such a case, conditions like the acute post-abortion or gonorrhoeal endometritis, beginning of metropathia haemorrhagica, prolonged defective desquamation or irregular shedding of the secretory endometrium described by Pankow, and rare cases of ectopic gestation or the corpus luteal Haematoma rupture must be borne in mind. It is at once evident that all these lesions except the acute endometritis require the removal of the cause by operative or some other appropriate method. The object of this paper is to deal with the medicinal line of treatment proper and hence no further details need be given regarding the operative line of treatment in these lesions associated with gross pelvic pathology.

The types of lesions which will be considered at length are those cases, which on P V examination give no appreciable abnormal findings and yet the patients are found to have a profuse blood loss at the time of each menstrual period. Such a condition one often sees at both extremes of menstrual life namely at puberty and at the approach of menopause and one may expect a similar type of condition during the first few periods following an abortion or a full time labour. The underlying cause

which is responsible for these abnormal clinical manifestations is the failure of adjustment of balance between the various hormones concerned in the phenomenon of menstruation, the pituitary-ovary-thyroid mechanism, being upset, very often leads to excessive blood loss. But all the cases must not be put down to hormonal disturbances as there are also other causes, e.g., defective function of the uterine musculature mainly in infantile and under developed uteri and also an additional factor of changes in the arterial walls and uterine musculature in cases of chronic subinvolution and chronic metritis. Other systemic diseases may also favour menorrhagia and they are high blood pressure, venous congestion due to cardiac decompensation and chronic pulmonary diseases and asthma, Cirrhosis of the liver and the group of blood dyscrasias like polycythemia rubra, purpura haemorrhagica, leukemia, aplastic or splenic Anaemia and sometimes even in simple achlorhydric anaemia. Thus it will be evident that the cases which require trial with medicinal and other lines of treatment before actually the diastic radical measures are adopted fall into a group which does not give abnormal findings on P V examination. That being so, one has, very often, to give a fair trial with the usual medicinal methods so as to regulate the functions of the uterus, endometrium, ovaries, or the other systems in the body which are directly responsible for the symptom of menorrhagia.

The general hygienic measures should be explained to the patient and well-balanced diet, rest and exercise in the open air should be instituted. Attention to the bowel movements particularly at the time of expected periods is helpful in relieving congestions of the pelvic organs and thus mild saline purges during the last week of menstrual cycle are found beneficial by the patient. The dietary deficiencies must be corrected by the administration of a liberal well balanced diet containing plenty of green vegetables with fresh fruits and milk. In non-vegetarian patients the improper nitrogen balance in the food must be adjusted. The associated severe anaemia in these cases of menorrhagia of long duration may require treatment with vitamin B complex, dry brewer's yeast, crude liver extract and arsenic either orally or preferably by parenteral route. The use of iron should be made with caution during the bleeding phase, but in between the bleeding free use can be made in the

form of ferri et ammonium citres gr 20 tds or Bland's pills gr 20 tds One must not fail to rule out the presence of any focal sepsis outside the genital organs as it may be responsible for causing increasing tendency to bleeding

In order to correct the faulty contraction and to improve the tone of the uterus the time honoured drugs like the oxytocic principles may be used They will be found useful in the cases of chronic subinvolution, chronic metritis, TB endometritis, undersize and infantile uteri and even in cases of fibroid and adenomatous polyp, too small to be detected by P V examination The prescription like the following is really worth a trial for few menstrual periods—R/Ergodex (BDH—dr Iss, Tr Hydrastis—dr iii, Tr Nucis Vomica—m 30, Syrup—dr VI, Aquae ad—oz VI, 1/6 part thrice a day Pulvis Calci Lactas gr XXX, TDS

During the actual severe bleeding the immediate effects may be secured by injections of Ergometrine or Neogynergen intramuscularly or even Ergometrine 0.125 gms intravenously repeated as required But it must be mentioned that the injection of Pituitary Extract 10 units or 1 cc is very rarely likely to be effective in all the cases of excessive menstrual loss although one often finds good results in cases of acute subinvolution and one type of metropathia haemorrhagica which is characterised by profuse uterine bleeding at exactly monthly interval In the latter condition the use of pituitary extract is merely empirical and has no pharmacological backing

Complete rest in bed and hot vaginal douches during the excessive blood loss may be in addition useful and in extreme cases vaginal packing may have to be resorted to as a temporary measure before the patient can be prepared for an operation

The other measures which may also be used in these cases are the use of substances which increase the coagulative property of the blood Thus calcium may be administered in the form of intravenous injection of 10% solution of calcium gluconate in 10 cc doses The intramuscular injections of Horse serum or some other preparation like Coagulin Ciba, Haemoplastin, Arihemapactin or Sangostop may also be used Gold-

berger and Peck secured very encouraging results with the use of Snake Venom, which has a direct effect on the walls of the blood vessels, making them more resistant to bleeding. The improvement in their cases lasted from 2 months to 4 years. The method to be used is as follows—Moccasin venom in 1:3000 dilution is given as daily subcutaneous injection starting with $\frac{1}{2}$ cc and increasing to one cc by the third dose. If the bleeding is very profuse one cc is given twice daily until the bleeding is controlled and then two or three times a week for 3 menstrual periods. If the patient is sensitive to foreign protein she can be desensitised by small doses of 0.05 cc the injection being repeated every fourth day and the dose may be increased to 0.3 cc.

10 cc of 10% solution of congo-red when given intravenously often checks the haemorrhage by its action through reticulo-endothelial system. The use of Vitamin K either in the form of biweekly injection or by oral administration during the second half of menstrual cycle may often help to reduce the blood loss during the subsequent menstrual periods. During the bleeding phase, however, the injections may have to be repeated daily. Vitamin C may be administered using 50 mgm doses intravenously or two intramuscular injections daily during bleeding.

Blood Transfusion has also its place in the treatment of menorrhagia especially in young unmarried girls in whom Dilatation with curettage cannot be resorted to quite readily. In such unfortunate individuals repeated small blood transfusions, say even 100 cc and preferably taken from a young healthy male adult or a pregnant patient preferably in the 3rd month of pregnancy may be used. The former's blood is likely to contain male hormone while the latter can give the chorionic luteinising hormone circulating in her blood in addition to blood serum.

The use of hormones, in the treatment of uterine haemorrhage must be made with utmost caution as its indiscriminate use is likely to upset the ovarian pituitary mechanism and thus produce dysfunction of the ovary by the improper treatment administered. If a physician is not well acquainted with the complicated hormone mechanism it is far better to refrain from

the use of the hormone rather than make the case complicated by their improper use. It must also be well emphasized here that the use of hormone without the preliminary biopsy study of the endometrium is really to be discouraged. It is no wonder that hormone treatment very often fails when biopsy study is omitted only because the right type of hormone is not used.

At the outset it must be emphatically expressed that oestrogen preparations have got no place in the treatment of menorrhagia. Hambleton reported the results of his treatment with huge doses of oestrogen during the first fortnight of the menstrual cycle following a preliminary curettage. But the effect of this treatment was to bring about complete inhibition of the Pituitary function and even failure of ovulation so that one may lead the case on to hyperplasia of the endometrium and a prolonged period of amenorrhoea. Moreover, the treatment itself is very expensive and is likely to upset the working of pituitary and ovaries.

Progesterone or Corpus luteal hormone is useful in those cases where there is failure of secretory phase in the endometrium. This depends upon the failure of ovulation which is likely to be encountered at the time of puberty during the first few years and at the time of menopause. At both these periods of life even if the patient may be menstruating regularly every month there may be associated menorrhagia and failure of ovulation as shown by endometrial biopsy study. These cases respond very well to treatment by Progesterone by controlling menorrhagia. That hormone can be given in doses of 2 mgm or 5 mgm intramuscular injections during the last week of the menstrual cycle and during the actual bleeding phase. Nowadays even oral preparations like lutocyclin tablets 10 mgm are available which are found effective inspite of the action of acid gastric juice. As stated previously the cases of subinvolution and chronic metritis should be treated with ergot preparations to tone up the uterus rather than with this hormone.

Male hormone preparations are really useful in the treatment of menorrhagia of functional origin especially at the time of menopause. The same treatment can also be used at the time of puberty provided the dose is well regulated. The hor-

mone controls the bleeding by its indirect action of inhibition of the pituitary and its direct action on the uterine endometrium and the musculature by producing atrophy in these structures. Stuges and Aborbanel, however, believe that the direct action on the muscle is the inhibition of rhythmic (oestrin) contractions thereby decreasing the volume of blood flowing to and through the uterus and the local action stimulates the myometrial elements about the arterioles constricting them and thus helping to control the blood loss. In short the end results of the action of this hormone are quite opposite to those produced by oestrin. The hormone should be given in the form of intramuscular injection 10 to 25 mgm daily till the bleeding stops. The total dose given during the period of one month should not exceed 200-250 mgm otherwise undesirable effects, such as hair growth on the lips, enlargement of clitoris, deepening of voice and other masculinising effects may be produced. Except the anatomical alterations in the larynx and clitoris, the rest of the manifestations usually disappear gradually on the stoppage of treatment.

Chorionic gonadotropic hormone (Antuitrin S) can also be used in cases for which male hormone and progesterone treatment was suggested. The dose required is very high, 200 units being given daily in the form of injections intramuscularly during the bleeding phase and the same hormone must be repeated during the second half of the menstrual cycles in the subsequent periods with smaller dose of 100 units every 3rd day. The treatment often proves expensive and results not certain.

Many cases with slight lower basal metabolic rate respond very well to thyroid treatment. The dose should be increased cautiously, using the patient's feelings and the pulse as the guide. As stated before the patients with low basal metabolic rate especially at the time of menopause are likely to suffer from menorrhagia and these respond well to thyroid treatment.

Now inspite of all these above mentioned methods of treatment if the patient is found not to improve in any way, the operative measures may have to be resorted to. The most popular operation of Dilatation and curettage may be undertaken and repeated as often as required provided there is no coexisting

active infection present anywhere in the genital track. The case of acute endometritis of gonococcal or post abortion sepsis are the ones likely to be missed and great harm may result even from this so simple an operation. During the child bearing period this operation is most useful but in elderly multipara upto the age of forty the vaginal subtotal or total hysterectomy without the removal of the ovaries may have to be performed in the end thus maintaining the functions of the ovaries. Patients over the age of forty alone are best treated by intra-uterine radium application or by x-ray. The former treatment is much to be preferred as the operator gets the opportunity to examine the uterine scrapings before introducing the radium while the x-ray treatment is likely to be carried out blindly without definite pathological diagnosis. If the cancer of the body is missed at this stage the appropriate treatment by the operative removal of the uterus may unnecessarily be postponed and the whatever little chances the patient may have in getting cured, may be lost.

The treatment of menorrhagia in unmarried girls or young adults is always a great problem and requires a careful handling of the case. As stated before, one has to postpone the operative treatment till the last and in the meanwhile full trial must be given to medicinal treatment as detailed above. But before submitting the patient to hormonal treatment a thorough blood examination must be carried out, including the blood-sedimentation rate, so as to rule out any blood dyscrasias or active tubercular and other septic conditions in the body. If the former condition is detected the exposure of the splenic area to Deep X-rays is often found beneficial in addition to general measures. But the use of small doses of Radium or Deep X-rays to the ovaries should on no account be hurriedly thought of in young patients since much harm may be done to the growing Ova and the hormone producing Granulosa cells. Even though a temporary stoppage of menses may be secured by small doses of 600 mgm hours radium exposure or an equivalent Deep X-ray exposures the possibility of foetal abnormality in the future pregnancies or even the development of regular anovular menstruation with permanent sterility must be explained to the patient and her relatives.

Mention must also be made of the intrauterine irrigation of glycerine for chronic cases of menorrhagia as it is worth the trial before one resorts to the drastic method of vaginal hysterectomy or radium application. This treatment was suggested by Hobbs especially for acute subinvolved uteri, but it can very well be applied in the most resistant menorrhagia cases. The irrigation may be carried out daily by introducing a very fine catheter into the uterus and injecting about thirty cc of glycerine, care being taken to see that the free outward flow of glycerine from the uterus is not hindered. There is a danger of production of shock if the uterus gets unduly distended, if the precaution mentioned is not taken or if glycerine pours into the peritoneal cavity along the tubes. The treatment relieves the oedema of the thickened endometrium and stops the bleeding.

In the end it must, however, be thoroughly emphasized that every menorrhagia case requires a thorough gynaecological examination before the medicinal treatment is started as unnecessary time and money may be lost in medical treatment in a case which requires immediate radical operation especially in the presence of malignancy, thus making the outlook and prognosis of the case miserable.

Critical Notes and Abstracts

BRONCHOGENIC CARCINOMA

Menne and Anderson review (J.A.M.A. Dec 27, 1941, p 2215) the incidence of bronchogenic carcinoma in the Pacific North-west and comment on 85 cases. After reviewing the literature on the subject and from a careful analysis of their own statistics, they conclude that there is both *a relative and an absolute increase* of the bronchogenic carcinoma in the Pacific North-west.

They describe two outstanding macroscopic types of bronchial carcinoma (1) *hilar nodular type*, and (2) *diffuse necrotic type* with a minimal of hilar involvement. To this may be added the *third type of apical carcinoma* originating in the peripheral bronchi which, owing to its invasion of the bones in the region of the upper thoracic aperture and of the nerves produces a very characteristic clinical picture (the so-called superior pulmonary sulcus tumor of Pancoast). This classification is similar to Aschoff's, who has described "(1) small nodular masses arising from bronchi of the first to the third order, and (2) the infiltrating type in which a large portion of the lung or an entire lung is involved."

Bronchogenic carcinoma occurs as often in the right lung as in the left, but is observed in almost twice as many upper lobes as lower lobes. Average age is 55, with a range of 38 to 77 years. The sex ratio is 13 males to 1 female.

The sequence of progress of the growth is as follows. *Hilar nodular type*—(1) hypertrophy and metaplasia of the bronchial epithelium, (Carcinoma in situ), (2) partial or complete occlusion of the bronchus, (3) extension through the bronchial wall, cell infiltration and fibrosis, (4) extension through the lymphatics, (5) involvement of the hilar glands, (6) limited and slow massive extension into the lungs.

Diffuse necrotic type—(1) hypertrophy and metaplasia of the epithelium (2) early invasion into peribronchial lymphatics with intra-pulmonary lymphatic stasis, (3) engorgement and thrombosis of blood vessels, (4) secondary lobular pneumonic infection, (5) diffuse carcinosis, (6) coagulation necrosis with multiple abscess formation, (7) bronchiectasis limited to terminal bronchi, (8) regional hilar node involvement, occurring late in the course of the disease. This type of carcinosis is characterised by spread through a definite lymphatic distribution in the lung as well as by continuity into tissue spaces. Pleurisy with effusion is more frequent with this type. Be-

cause of the earlier and more diffuse involvement of the lymphatics and blood vessels, distant metastases are more common in this type.

Of the *clinical aspects* the authors stress the fact that the symptoms of bronchogenic carcinoma are widespread and variable. Two sets of symptoms and signs, those referable to the lungs and those arising from metastases in organs and tissues outside the chest must be recognised. They give the following table of the frequency of various symptoms and signs with the two types of bronchogenic carcinoma in 14 cases in which autopsy was done.

TABLE I

	BRONCHOGENIC 29 Cases	CARCINOMA 15 Cases
	Diffuse Nodular type number	Diffuse Necrotic type number
Cough	8	4
Cough with expectoration	19	9
Haemoptysis	14	1
Dyspnoea	18	6
Pain—Mediastinal	6	0
—Pleural	1	7
—Intercostal	1	0
—Unspecified	6	2
—Other than in chest	7	1
Atelectasis	11	3
Empyema	2	1
Pleural Effusion	5	5
Abscess of lung	5	1
Congestion of lung	2	1
Haemothorax	2	3
Hoarse Voice	0	3
Cerebral & Spinal signs	6	0
Ascites	1	0
Loss of weight & Weakness	8	1
Haemopericardium	1	0
Pancreatic fat necrosis	1	0
Lymphatic & Venous obstruction	1	0
Total cases studied	29	15 = 14 cases

It will be seen from the table that approximately half the patients with hilar nodular carcinoma presented symptoms referable primarily to lungs, while an equal number had symptoms attributable to metastasis. On the other hand, of the patients with diffuse necrotic carcinoma twice as many had symptoms traceable to metastasis as had symptoms referable to the lungs. Lung symptoms occur more frequently in the earlier stages of the disease and are more common in patients with hilar nodular carcinoma. The symptoms and signs resulting from pleurisy, abscess, empyema, haemorrhage, dyspnoea, cough, hoarseness, aphonia, and spinal cord and brain involvement are more frequent with diffuse necrotic carcinoma.

AMENORRHOEA

Zondek (JAMA Feb 28, 1942, p 706) suggests a new *simplified method* for the treatment of amenorrhoea as follows

1 For secondary amenorrhoea of more than two years' duration, a total of 50 mg of progesterone distributed over from two to five days (Injection of 10 mg daily for 2 to 5 days)

2 For secondary amenorrhoea of less than two years' duration, the same dosage or a total of 25 mg of progesterone with from 2.5 to 5 mg of estradiol benzoate distributed over two days

3 For primary amenorrhoea and castiation amenorrhoea, a total of 50 mg of progesterone with from 2.5 to 5 mg of estradiol benzoate distributed over five days (Injection of 10 mg and 2.5 or 1 mg daily for 5 days)

A further simplification will be possible by the oral administration of pregnen-inonol instead of progesterone

POTASSIUM SALTS AS DIURETICS

Potassium salts have been used as diuretics for generations, but at present after the advent of the mercurial diuretics there is a tendency to ignore them. Wilks and Taylor used potassium nitrate as a diuretic in 1868, and Magnus Levy and Barker used potassium chloride in 1932. Since 1932 Keith has demonstrated the diuretic action of potassium salts—chloride, nitrate, bicarbonate, acetate,—given by mouth to normal men. The kidney is able to concentrate the potassium delivered to it by the blood serum, approximately fifty times. After bicarbonate, acetate and citrate salts of potassium, the reaction of urine is invariably more alkaline. Potassium nitrate causes a relatively greater diuresis and greater increase in the excretion of chloride and sodium than any of the other salts. Potassium chloride was next in efficiency. With potassium nitrate or chloride it is possible to produce diuresis in about 80% of the cases, only 20% fail to react.

The dosage necessary to produce diuresis is greater than what is recommended in the pharmacopoea. The initial daily dose of potassium chloride is 9 Gm (gr 45 tds), and that of the nitrate and the bicarbonate 12 Gms (gr 60 tds). A 10 per cent solution of the salt can be given by mouth without discomfort, except epigastric burning sensation or nausea.

The potassium salts can be used in cardiac oedema as well as in renal oedema. Small doses of potassium chloride should be tried at first to avoid toxic effects in cases of cardiac oedema. In renal oedema, potassium salts should *not* be used when there is marked renal failure, as shown by extreme oliguria, or anuria or a value of urea in the blood higher than 80 mgm per 100 cc of blood.

The following two cases show the effect of potassium nitrate (gr 30, 45 to 60 tds) by mouth, in cases of subacute nephritis —

Case 1 A boy aged 16, diagnosed chronic parenchymatous nephritis, (6 Oct, 1942 Ind Reg No P/9591 K E M Hospital), was treated with the usual non-mercurial diuretics without any result. He was put on potassium nitrate, 30 grains four times a day. This produced a profuse diuresis, the amount of urine passed in 24 hours

being 75 to 105 oz., and his weight fell from 145 lbs to 85 lbs (a loss of 60 lbs) in two weeks, and remained steady on potassium nitrate gr 30 three times a day. He was discharged after a fortnight as the oedema did not return.

Case 2 A man, aged 49, diagnosed nephrosis was put on potassium nitrate grains 30 four times a day at first and then one dram three times a day. There was marked diuresis and the weight fell from 151 lbs to 134 lbs in a fortnight, a loss of 17 lbs. No other treatment was given except a salt-free diet and an occasional pulv glycy Co.

MODIFIED MALARIA FLOCCULATION TEST

Among the present-day laboratory methods in the diagnosis of malaria, the seroflocculation tests are the simplest, involving little labour, equipment and personnel. The earliest test was introduced by Henry (1928) based on the property of the malarial serum to flocculate a solution of melanin pigment derived from the chorioid of ox eyes. This original test was intricate and has been given up. The exact chemical nature of the reaction is still not understood.

This test was modified by Wisemann (1934). He observed that when malarial serum was added to distilled water, a precipitate occurred. It was observed that the reaction with the water was, in fact, more reliable and much simpler than the original Henry's test.

V R Naidu, A V Rao and Rajagopal, while carrying out the malarial flocculation test in the laboratory at the Krishnarajendra Hospital, Mysore, with distilled water, observed that the accidental contamination of the distilled water with small quantities of ethyl-alcohol sensitized the reaction to a great extent.

This is the basis of the modified malaria flocculation test which is described below —

Technique of the test The blood—two cubic centimeters of venous blood are drawn from the patient's vein with all aseptic precautions, preferably using the syringe in sterile normal saline to prevent haemolysis. The blood is placed into a clean small dry test tube and allowed to clot at room temperature. When the test is required to be done in haste, the serum is separated by centrifugalisation. The sera in all cases are required to be clear.

The test solution The solution is prepared freshly every day by adding 1.5 c.c. of absolute alcohol to 8.5 c.c. of freshly prepared distilled water.

The actual test Two clean test tubes roughly measuring 8 cms in length with an internal diameter of 8 mm are taken. One is filled with normal saline approximately $\frac{3}{4}$ th full and serves as control. The second test tube is filled to the same level with the freshly prepared alcoholic solution. Two drops of the clear serum to be tested are added by means of a clean glass pipette to each of the tubes. The two tubes are inverted twice or thrice to allow thorough

mixing of the sera In most of the cases the opalescence appears immediately as the serum diffuses through It is wise, however, in doubtful cases to read the results after standing the tube for half an hour at room temperature The reading is best done by day light

Results A comparative study of the flocculation test (M F) was made on 300 patients of the Krishnarajendra Hospital Of these 207 gave a history of recent malaria

TABLE I

Solutions	Number positive	Number of Cases Tested	Percentage
Distilled water	122	207	59.0
Alcoholic Solution	175	207	84.9

As a control group, a series of 93 in patients admitted for various surgical conditions were examined similarly who denied the history of malaria within the past one year

TABLE II

Solutions	Number Positive	Number of Cases Tested	Percentage
Distilled water	14	93	14.8
Alcoholic	20	93	21.5

The reaction is negative in the early part of the disease and becomes positive with the administration of anti-malarial therapy, from a week to ten days later

The value of a negative flocculation is quite high, provided the result is confirmed by a subsequent test 10 days later

Book Reviews and Notices

- 1 THE NUTRITIVE VALUE OF INDIAN FOODS AND PLANNING OF SATISFACTORY DIETS (Revised and enlarged 3rd edition, 1941) Health Bulletin No 23 pp 50 Price as 2/-
- 2 RICE—Health Bulletin No 28 pp 22 Price as 2/-
- 3 FOOD AND DIET—WRITTEN FOR CHILDREN, Health Bulletin No 30 pp 20 as 3/-
All published by the Manager of Publication, Government of India Delhi
- 4 THE FOOD SUPPLY by Radhakamal Mukerjee, pp 32 Price as 4/-, published by Oxford University Press, 1942

These excellent pamphlets should be more widely known to the physicians They describe the modern conceptions of Nutrition in simple language for general readers The views given there are authoritative and no exception can be taken to them The table of food values given of Indian foods is exhaustive and up-to-date and

should help physicians to prepare diets for their patients. The pamphlet on RICE contains a wealth of information much of which will be news to many a physician. We feel that every doctor or educated man should read this pamphlet on Rice—the staple cereal for 700 million people or approximately half of the world's population. The third pamphlet entitled FOOD AND DIET is written for children and should be read in every school as a compulsory lesson. We congratulate W R Aykroyd of the Coonoor Nutrition Research Laboratory on the production of these useful booklets.

Radhakamal Mukerjee's pamphlet is written from an economist's point of view and deals with the production and distribution of food and enumerates 10 features of progressive food policy, which, if followed by an enlightened government, will solve our food problem. It also discusses the food shortage in war-time and recommends practical measures for the government, which are very timely.

ENDEAVOUR—A quarterly review designed to record the progress of the sciences in the service of mankind. Published by The Imperial Chemical Industries, London. Vol I 1942 Nos 1, 2, 3, 4. Price sh 5/- each.

We welcome this new venture which is brought out during the war period to encourage scientific workers and to make the result of their labours known far and wide, and we wish it every success. The journal is designed for the general scientific reader, and is not meant for the specialist. As the Editor says, "Science is not the product of any one race, or of any one age." All races of man, provided sufficient opportunities are given are likely to contribute to natural knowledge. We, in India, who are supposed to be less scientific-minded and more philosophically inclined to vague generalisation and imaginings, have also shown sufficient scientific aptitude during the last generation or so, and contributed magnificently to various branches of natural sciences. Of all intellectual workers, physicians are supposed to be the least scientific and least interested in other branches of natural science. This is indeed unfortunate, for a physician is a naturalist par excellence, and though humanism is a part of his work, he can hope to achieve little, if his work is not based on scientific principles. The contributions which other sciences such as chemistry, physics, and biology, have made to advance medical practice are enormous, and modern medical practice and progress are impossible without the help of these basic sciences. "The Manufacture and Use of Vitamins", "Disease-resistant plants", "The action of x-rays on living cells", "The Progress in bacterial chemotherapy", "Vegetable drugs of Britain", "The physicist aids the physician", are some of the articles in these issues which will demonstrate this fact to the readers. There are also excellent articles on heredity, agriculture, animal husbandry, etc., which will interest physicians. We believe this journal will be as useful to diffuse scientific knowledge as the NATURE and we hope that it will be read widely in India.

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Let us remember

CLINICAL DESCRIPTIONS AND CASE SHEETS FROM RAMAYANA

By

D V S REDDY,
Andhra Medical College, Vizag

The epics of the West have been closely studied with a view to learn new facts regarding diseases and deformities of antiquity. No attempt seems to have been so far made to apply scientific methods of medical history to the great epics of India. In this brief article some of the interesting case reports and clinical descriptions are brought together and presented to the physicians who may solve some of these medical puzzles for the benefit of Medical History.

Case History of Dasaratha's Fatal Illness

When Kaikeyi, in harsh language, addressed the King Dasaratha goading him to send Rama to the forest, the King was "deprived of his senses and felt a sensation of whirling". He beseeched her not to press him to do this act. At last, when he was cleverly caught in the trap set by her, he "dropped down like a felled tree". The poet adds "And the Master, deprived of his senses, was like a woman or a patient with his faculties bewildered". Again, a little later, Dasaratha, trying to catch hold of Kaikeyi's feet, fell down in a swoon "like one enfeebled with disgrace". When Rama, who was sent for, found Dasaratha with tears in his eyes, and unable to talk, except uttering the word "Rama," the son was perplexed and asked Kaikeyi "Is he subject to any physical or mental disturbance?" Later, after going to Kausalya's apartment,

Dasaratha complained that he could not see her standing before him and asked her to touch him with her hands "My sight having followed Rama, doth not return yet" Then, he lay down, stupefied Finally, he complained "I do not perceive subjects of hearing, feeling or taste My senses are growing dim in consequence of mental stupor, like the rays of a lamp, reduced to smoke, becoming dim when the oil has been exhausted" The poet relates that at midnight, the King, wrought up, with the violence of emotions departed his life These ladies tending on the King, became apprehensive of King's life, "knowing the condition of the sleep, feeling him, as he lay in his bed, did not perceive any action in the evermoving pulse" [*Hypertension and Coma*]

Case History of Kumbhakaina

Kumbhakaina, the brother of Ravana, was a creature fully under the sway of sleep some times sleeping away for 7, 8, 9 or 10 months At the time Rama was destroying the army of Ravana, Kumbhakaina had slept for 9 months The poet describes that he was lying looking like a hill extended and sunk in profound slumber The procedures and great efforts made to awaken him are fully narrated—but much exaggerated First, they smeared his body with sandal and made him inhale perfumes and aromas of wreaths and filled the place with incense of Dhupa Next, they began to make a mighty din rearing around him blowing cencches, and striking their arms with their hands Then, they took up maces and clubs and beat him with them Horses and camels, mules and snakes trampled his body Rakshasas prodded him with rods, lashes and hooks Simultaneously 1,000 kettle drums were sounded Even then, Kumbhakaina did not show any signs of awakening Then, strong Rakshasas armed with pemaids and maces and Satagnis attacked his body—all in vain It was only when 1,000 elephants rushed against his body that he regained consciousness He awoke and suddenly got up He was suffering from pangs of hunger He yawned again and again His relatives had learnt by experience how hungry he would be on waking and had made full preparations They pointed out to him the heaps of rice, flesh of animals and jars of blood and other viands. He ate and drank all these and then only enquired why he was disturbed in his sleep But is that ordinary sleep? Two

explanations are given for the extraordinary and long slumber Ravana observes "that Kumbhakarna was deprived of his senses through lust and sleeps secure" The poet supplies a brief case history As soon as Kumbhakarna was born and was a babe, he began to devour up creatures by thousands Other creatures afflicted with fear, sought the refuge of Sakra, who smote Kumbhakarna with his bolt This probably did not deter Kumbhakarna Therefore, when the Lord of all creation, Brahma was informed of the ravages of Kumbhakarna, the great father cursed him "From this day forth thou shalt lie down as one dead" Thus cursed, the Rakshasa fell down before Brahma But, Ravana appealed to Brahma, who then modified his curse "Having slept for six months, he shall wake for one day" [*Narcolepsy, Hypothalamic Tumor, or Sleeping Sickness*]

Sun-stroke and Sun-burn

Sampathi, brother of Jatayu, narrates the story of their misadventure From pride of power of flight, the eagle and his brother began to voyage the skies, afar off, with a view to testing each others prowess—vowing that they would follow the sun After flying for a while, very high, the birds began to sweat, became bewildered and fainted frightfully "We knew not the South or the West My mind, combined with my eyes, grew feebler, and my wings blasted and rendered inert, I fell on Vindhya Hill" When they were both flying high and Jatayu went too high up against the rays of the Sun, he became faint and stupefied—struck by solar rays So, Sampathi shadowed his brother with his wings Thereat, Sampathi's wings became scotched and he too dropped down He did not know what happened to Jatayu and lay senseless for six days, gradually regaining consciousness afterwards Old Sampathi adds "I knew the realms of Varuna the wars of Gods and Asuras and the churning for Ambrosia"

Endocrine Disorders

1 The story of Tataka is a case of endocrine dysfunction and deformity Visvamitra relates to Rama that Suketu, a Yaksha, had a daughter endowed with great strength When she had grown and attained youth and beauty, she was married to Sunda and gave birth to a son When she tried to devour Agastya, the saint cursed her "O, Yakshi, since in frightful guise with a frightful face, thou hast desired to eat up a human

being, do thou immediately leave this (the original) shape and become of a terrible form" When Rama saw her, she had hideous visage and colossal proportions "The sight of her stricken terror into the hearts of even the brave" (Vol I, p 67)

2 Grimvisaged rakshasi Ayomukhi is described thus "Having a formidable figure, causing fright, having a huge belly, a high person and rough skin looking fearful with dishevelled hair" (Vol I, p 671)

3 A man-eater, Viradha, a Rakshasa, is described as follows "Resembling mountain summit with hollow eyes, a huge face, frightful, having a deformed belly, disgusting, dreadful, cyclopean, mis-shapen, of horrible sight . with his mouth widely extended" (Vol I, p 507)

Diseases of Limbs (Bones and Joints)

Kucanabha begot 100 daughters on Gitachi "They were endowed with youth and grace, perfect in limb and unparalleled in beauty The Air-God wanted them to become his wives but they replied that they had to obey orders of their father Air-God was enraged, and so "entered into their bodies and broke their limbs" "Their bodies being thus broken by air, these damsels overwhelmed with shame, with tears in their eyes, went to their father, who, finding his supremely beautiful daughters with their limbs broken and woebegone, asked, "Who is it that thus disregards Virtue?" "By whom have ye all come by this crooked form?" The girls replied that the Air-God was desirous of having recourse with them in an improper way and as they refused to agree, he handled them roughly" Then, he bestowed his daughters in marriage on Brahmadata, son of the sage Chuli and the Gandarbi—Somada—"And as soon as he touched them, the hundred daughters were cured of their crookedness and became free from anguish and endowed with pre-eminent beauty" And their father became delighted to see daughters freed from Air-God's wrath The question arises whether all these girls had their limbs broken by violence or whether the limbs bent and broke as a result of nutritional deficiency or whether all this is only a way of saying that these girls were affected by Rheumatism—a manifestation of derangement of Vayu (Air-God), The fact that all of them suffered simultaneously and all recovered suddenly is a good clue. (Vol I, pp. 83-85)

Sterility

No sons were born to Maheswara and Parvathi, for a long time Uma's curse of sterility on celestials is very revealing "While in association with Mahadeva for obtaining sons, I was broken in upon by you For this you shall not yourself be able to beget offspring on your wives And from this day your wives shall remain without issue" Even Brahma grandsir of all creatures told the celestials that sons will not be born "unto you of your own wives" (Vol I, pp 90-93)

Fits and Premature Birth

As the God of Fire was not present when Uma cursed the celestials, Brahma suggested that the Fire God may beget a son of Ganga—a son who will be the generalissimo of celestial forces Then, Pavaka approached Ganga saying "Do thou bear an embryo" And the Pavaka discharged his energy into her Ganga then spoke as follows "I am incapable of sustaining this new burning energy of thine I am burning with that fire and my consciousness fails me" Then Agni told Ganga "Do Thou bring forth thy embryo on this side of Himavath" Hearing his words Ganga cast her exceedingly affluent embryo on her streams And when son was born by the command of Indra, the Krithikas (stars) began to suckle him (by turns began to give milk to him) The Krithikas bathed the offspring that had issued from the womb As he issued from Ganga's womb he was called Skandha and as he was looked after by Krithikas he was also named Karthikeya The teats of Krithikas were filled with milk and assuming six mouths, the infant began to suck milk from the six ladies (Vol I, pp 90-93)

Multiple Birth

Sagara, with his two wives, had no issue for a long time After some penances he obtained a boon for a issue The eldest wife bore a son while the younger "brought forth a Gourd" "When it burst open, out came from it sixty thousand sons and nurses fostered them by keeping them in jars filled with clarified butter, and after a long lapse of time they attained youth" (Vol I, pp 94-95) [The Gourd is a caul containing sextuplets]

Attempt at Abortion by Poisoning

In narrating the geneology of Ikshwaku, Vasista mentions a medical story Asita, son of Bhageeradha, died leaving his

two consorts who were in the family way With the intention of destroying the embryo of the other, one of these administered poison mixed in food The lady thus poisoned saluted sage Cyavana and prayed for a son The sage said "In thy womb will be born an excellent son mixed up with poison, highly powerful, energetic and strong" This son was no other than the great Sagara (Vol I, p 160.)

Food Poisoning or Poisoned Food

In the story of wily brothers Vatapi and Illwala, taking the form of Brahmins and speaking Sanskrit, used to invite Brahmins to Shraddhas And cooking his brother, wearing the shape of a sheep (and probably adding some poison), Illwala used to feed Brahmins according to rites Then when the Vipras had fed, Illwala used to say, "O, Vatapi come out uttering a loud sound" Hearing these words, Vatapi bleating like a sheep came out tearing their bodies" In this way, thousands of Brahmins were destroyed and it came to pass that Maharshi Agastya came to Shraddha and was fed as usual But, when the Asura said to his brother, "Come out" the all-knowing Agastya laughed and said that the meal is well digested and no more would his brother kill Vipras and come out (Vol I, p 530)

Original Contributions

PROSTATIC ABSCESS

By

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Common observers reason from the progress of the experimental sciences to that of the imitative arts. The improvement of the former, however, is gradual and slow. Much time is spent in collecting materials, still more in separating and combining them. Even when a system has been formed, there is to add, to alter, or to reject. Every generation enjoys the use of a vast hoard bequeathed to it by antiquity, and transmits that hoard, augmented by fresh acquisitions to future ages.

Urology probably represents the most progressive and successful branches of surgery. The advent of x-rays, followed by other diagnostic aids, such as retrograde pyelography and uroselectan, have rendered it a comparatively safe and sure procedure.

France can, rightly, claim pre-eminence as the birthplace of genito-urinary surgery, but French books, like Frenchmen, are engrossed in a sentimentality which, though pleasant in politics and poetry, lacks the harsh commonsense that is the hall-mark of good surgery.

To English surgeons one can give the full credit of having imbued into the study of the subject the essential delicacy and persistence. However, it was Guyon (34) from France, who struck the first successful blow to the stake that signalled the entrance of urology as an important and integral part of surgery. His pupil Albarran, was also interested in urology, particularly in its relation to diseases of the prostate.

The majority of surgeons regard the subject of prostatic abscess as a very trite one, and consider it, solely, as an uninteresting complication of acute specific urethritis. The falsity of such a conception can be easily proved by but a cursory review of the subject.

For instance there is the unique case described by Harlow

Brookes (12), who tells of a young man that presented symptoms so unequivocal of paratyphoid fever, that this condition was diagnosed by several eminent physicians. It was only late in the disease, when slight perineal discomfort lead their attention to the prostate, that a large prostatic abscess was found to be present. The abscess ruptured into the urethra, and the patient made a rapid recovery.

Kitchmei,⁵⁰ in an excellent resume of forty-three cases observed by him, reports a case of metastatic abscess following osteomyelitis of a finger. Following this is the interesting case, described by Lydston,¹⁶ where the condition so closely simulated prostatic hypertrophy that even at suprapubic cystotomy it was unsuspected, till spontaneous rupture of the abscess occurred during a period of bladder drainage. These three simple cases show that a prostatic abscess may occur in any general toxic condition in which there is no evidence of past or present history of gonorrhoea.

Randall,⁷³ writing in the *Annals of Surgery*, reports eight cases that were non-gonococcal and eight in which gonorrhoea was present. Bugbee,¹¹ reports five cases of influenza in which prostatic abscess was a complication. Alexander Randall⁷³ writes a case in which the pain caused by a prostatic abscess was radiated to the groin and closely simulated a hernia. All these cases serve to indicate how readily the aetiology and symptoms of prostatic suppuration can deviate from the normal, and thus broaden the field calling for a differential diagnosis.

Anatomy

A brief description of the more salient features of the anatomy of the prostate is germane at this point, for, it is at the portals of "Anatomy" that lie the basic elements of the pathology, diagnosis and treatment of any surgical condition.

The prostate is a solid organ, partly muscular and partly glandular. It embraces the neck of the bladder and the first part of the urethra. Transversing the gland are the two ejaculatory ducts which open into the urethra.

The prostate consists of fifty to sixty small glands, whose ducts open into the urethra, twelve to fourteen of these glands lie in a loose stroma of their own, which radiates from the posterior aspect of the urethra to join the capsule of the gland, these are called the 'posterior lobe'—the 'true prostatic glands' of the Continental writers. They form the whole of the posterior

surface and the greater part of the lateral surfaces of the prostate. Their ducts, larger and longer than the others, converge to open around the orifice of the utriculus masculinus.

The remaining prostatic glands lie in the dense muscular tissue around the urethra and are called the 'peri-urethral glands' or 'central gland' (Albarran and Motz¹)—according to their situation they are divided into four groups or lobes. Two lateral (fourteen to sixteen in number) whose ducts open into grooves on either side of the crista urethralis, middle, (eight to ten) opening into the urethra above the utriculus masculinus, and anterior, (four to six) which open into the anterior wall of the urethra. The latter group may, occasionally be absent.

Abarrans glands, a few small glands opening into the posterior wall of the internal meatus, are often continuous below with the middle lobe.

Whilst the lateral, middle and anterior lobes are continuous with each other, the posterior lobe is partially separated from them by the outermost layer of plain muscle, sometimes incomplete, which surrounds the urethral musculature and is continuous above with the vesical sphincter. The term "periurethral glands" applies, therefore, to the lateral, middle and anterior lobes, and the application of this name to small submucous crypts in the prostatic urethra is wrong and misleading.

The prostate is closely covered by a thin fibrous "prostate capsule". Outside the capsule, surrounding the gland is the "prostatic sheath". It originates from the pelvic fascia and is exceedingly strong. It is a matter of importance to note that the prostate lies loosely in this sheath. Only in the medium plane, in front, and around the urethra as it emerges from the prostate is there any semblance of adhesion between the prostate and its sheath. The sheath is of great strength and its unyielding nature probable accounts for the great pain occasioned in the acute form of prostatic suppuration.

Pathology

A consideration of the pathology of prostatic abscess soon reveals its close association with gonorrhoea. A prostatic abscess may, however, occur entirely independently of any such infection. Only seventy-five per cent of the cases observed by Sargent and Irwin⁸³ had a history of gonorrhoea. In the opinion of G. H. Thomas of Minneapolis²⁷ fifty per cent of the cases of prostatic abscess are due to bacteria other than the gonococcus.

An abscess may form as a complication of faulty catheterisation, typhoid fever,¹² appendicitis,⁹⁷ prostatic calculi (case 2), influenza,³⁵ mumps,¹⁰⁵ or any form of general sepsis. Straminger reports three cases of Staphylococcal abscess subsequent to a septicaemia following anthrax.

From these facts one realises that a prostatic abscess can originate from two sources—namely, direct infection and metastatic infection. The question of tuberculous prostatic suppuration is not considered here, because it is too wide and complicated an entity to be discussed in this brief paper.

The direct infection usually results from faulty catheterisation or gonorrhoea. Cabot¹⁷ discusses, in the *New England Journal of Medicine*, a fatal case of prostatic abscess following 'tying-in' of a catheter. Maelsch found prostatic involvement in ninety-four per cent of cases of acute specific post-urethritis under his care, but Sohnen³⁰ from the extensive material at Eilanger reports but three cases.

The second type occurs as a metastatic involvement of the gland from some distal focus of infection.

Girling Ball⁵, reports two cases of metastatic staphylococcal abscesses.

1 A medical student, aged twenty-four, who had suffered, for a few weeks, from boils on the neck and buttocks, and had had a septic finger, was suddenly seized with throbbing pain in the perineum and difficulty in micturition.

Per rectum, the prostate was enlarged, smooth, tense, soft in the centre, and fluctuant. The mucosa of the rectum was not affected. No urethritis or stricture was present. The leucocyte count was 8000-9000.

An abscess was diagnosed and successfully opened via the perineum.

2 A male aged fifty-one, developed a boil on his scalp. A few days later, whilst the boil was still present, he had a rigour. There was no pain on defaecation. A prostatic abscess was found to be present and drained via the perineum.

Kretschmer,⁵⁰ in 1920, also recorded a case of metastatic prostatic abscess following osteomyelitis of a finger. Strominger⁹⁵ mentions a case in which prostatic suppuration was a complication of mastoiditis.

Abscess formation in the prostate may also result from severe renal or vesical infection.

A patient, aged forty, some eight weeks after an operation for drainage of a left perinephric abscess, complained of pain and tenderness in the perineum. This together with the acute retention, drew attention to the prostate. An abscess was diagnosed and drained through an incision in the rectum. (A fuller report of this case is appended at the end of the paper)

Cases have been recorded where prostatic abscess followed sudden decompression of a distended bladder. Keyes cites cases of prostatic suppuration which were the result of long-continued prostatism. He regards this as an exceedingly uncommon complication of that condition.

Prostatic abscesses are divided into two groups, depending on whether the suppuration is intra-prostatic or peri-prostatic.

1 Intra-prostatic abscess. Leguen⁵⁹ and Mc'Carthy⁶⁴ proceed to further subdivide this group—

a intra-follicular

b interstitial

and in reference to their position—

a central

b cortical

c submucous

Primarily, the abscess is localised to the follicles and produces follicular prostatitis (Finger), which can clinically, be associated with catarrhal prostatitis.

Thence the suppuration spreads to the periphery of the follicle, and gives rise to a miliary abscess.

The coalescence of several miliary abscesses gives rise to the usual large prostatic abscess. These are often several in number, forming two to eight large, irregular cavities, which are separated by thin septa.

According to their point of origin, these abscesses may be situated more or less near the urethra, they usually however, in the later stages, tend to spread towards the urethra. They ulcerate the urethral mucous membrane and rupture into the urethra. Lafont⁵³ records that over seventy-five per cent follow this course.

Through the centre of this area of suppuration run the two ejaculatory ducts. These are invariably destroyed, and the infection often spreads to the seminal vesicles.

If the abscess spreads to the periphery of the gland, then it may burst into the periprostatic tissue and give rise to a periprostatic abscess

Periprostatic abscess A periprostatic abscess need not, as a rule, be secondary to an intra-prostatic abscess, it may arise from infections of the vas deferens, seminal vesicles or a plebitis (Gazy) It may even arise as a result of peri-urethral suppuration Minet⁶⁷ reports eight cases in which the prostate was entirely free from abscess formation, even though it was in the midst of a large periprostatic suppuration

It may be situated on the sides behind or above the prostate

a Lateral periprostatic abscesses are rare, and easily spread to the ischio-rectal fossa

b Retroprostatic abscesses are commoner, and they usually lie behind the prostatico-peritoneal membrane in the pre-rectal space

c A supraprostatic abscess probably represents the commonest situation The pus is localised between the seminal vesicles, behind the bladder, in front of the prostatico-peritoneal membrane and above the prostate

These elusive abscesses must be carefully searched for, and separately opened, undiagnosed, they easily spread and may even cause gangrene of the seminal vesicles ⁶⁹

The eventual course of the abscess is usually regular The intra-prostatic suppuration nearly always bursts into the urethra A periprostatic suppuration, however, is very likely to burst into the rectum or ischio-rectal fossa Von Blum ¹⁰ reports one case in which the abscess appeared as an enormous tumour over the symphysis, simulating a distended bladder Segond ⁸⁴ in 1880 described migrations to be inguinal, obturator, femoral, umbilical and para-rectal regions In these days, thanks to the early intervention of surgery, these complications are rarely seen

Symptoms

On the subject of symptoms, much or little may be said At first glance it appears rather a trite subject Unfortunately such is not the case A prostatic abscess may divulge its presence by acute symptoms settling down on a prostaticitis During the course of an acute prostatitis, however, there is a period of some days in which the condition seems to remain "in status quo," and it may be impossible to decide whether an abscess has formed Legueu ⁹⁵, Lydston ²⁶, and Herman and Carp ⁴³, divide the

symptoms into two groups, depending on whether the suppuration is acute or chronic

a acute the aching pain of prostatitis is replaced by a very severe, throbbing pain which is usually situated in the perineum, but may radiate down the thighs. In some cases the pain may be referred to the supra-public region, and there simulate a cystitis. Ball⁵ remarks that the commonest symptom is retention. The temperature rises, but is rarely above 102°F (Keith). The patient suffers from sweats and his complexion becomes sallow. Pain on defaecation is usually present, and may be so severe as to cause complete constipation.

There appears to be no age limit for the formation of prostatic abscess. Campbell¹⁸ reports a case of gonococcal prostatic abscess in a boy aged twenty-eight months. This case is of interest in that it is, I believe, the youngest one on record.

b chronic prostatic abscesses these are occasionally only discovered at autopsy, in the centre of a hypertrophied prostate (Saint Cene)²⁶. There are cases whose evolution is entirely silent and deprived of painful sensation. They may open into the urethra spontaneously, or are opened in the course of catheterisation. Urethral suppuration probably represents the only possible guide to such an abscess.

In other cases, an acute or sub-acute epididymitis may lead to a closer examination of the prostate.

A sudden rise of temperature in a patient with a "tied-in" catheter should also lead one to examine the prostate.¹⁷

These chronic abscesses develop quite easily in prostatic hypertrophy, and are usually impossible to diagnose because they give rise to no symptoms.

Diagnosis

The diagnosis of an acute prostatic abscess is often quite easy, owing to the presence of the characteristic symptoms,—acute retention, severe pain in the perineum and pain on defaecation. Physical findings, however, present difficult variances, and may often mislead the unwary clinician.

In a case of acute prostatitis we should always bear in mind the possibility of abscess formation. Both conditions may give rise to acute retention.

In acute prostatitis the gland is uniformly enlarged and not excruciatingly tender. The temperature is rarely high and the patient does not appear to be gravely ill. With the development

of a prostatic abscess the prostate suddenly increases in size, fluctuation, per rectum, is present in an abscess, but absence of fluctuation however, should never make a surgeon rule out abscess formation, because the suppuration may be deeply situated within the gland. The patient becomes acutely ill and the temperature may be as high as 102°F. Girling Ball emphasizes that the presence of a leucocytosis is an important sign in favour of an abscess formation. He cites the interesting case of a thirty-three years' old man who repeatedly showed a leucocytosis of 15,000 per c mm during the development of a prostatic abscess.

With the formation of a peri-prostatic abscess the swelling becomes boggy and more diffuse. Leguen⁵⁹ states that a constant finding in early peri-prostatic infiltration is the presence of a transverse band of tissue felt per rectum in the region of the prostate.

The following case is worthy of interest in that a common cause of perianal suppuration of prostatic and vesicular origin is frequently overlooked and seldom recognized.

"A man, aged fifty-two years, complained of dysuria and frequency of micturition for the previous four weeks. It was soon apparent that this was due to posterior urethritis not responding to the ordinary line of treatment. On admission to the hospital his temperature was 98°F, pulse rate 65, and respiration 20 per minute. The urine contained albumin, pus and some threads. A rectal examination revealed an enlarged prostate with a soft boggy mass high up on its right aspect. An operation was performed five days later when the prostate was exposed by the perineal route. There was much perirectal thickening, and an abscess cavity, containing about three drachms of thick caseous pus was found high up on the right side of the prostate involving the right seminal vesicle. A rubber drainage tube was inserted into the wound and the patient returned to the ward. On examination the pus was sterile, and the microscopic examination of some granulomatous scrapings showed no giant cells. Urine analysis, revealed no evidence of Tubercle Bacilli. The abscess drained freely, and the patient made a good recovery, being discharged healed in three weeks. It is evident that without adequate drainage the abscess would have tracked downwards and caused one of the common types of peri-rectal suppuration."

In cases of chronic prostatic abscess, the presence of an intractable discharge should always lead one to suspect the condition. Urethroscopy always reveals small beads of pus lying at the mouths of the prostatic ducts. Prostatic massage per rectum usually causes the appearance of a discharge at the meatus. The miliaary abscesses in the neighbourhood of the urethra only pour occasional drops of pus into the urethra and almost invariably remain undiagnosed. Desno²⁹ reports cases of sub-mucous abscesses which occasioned the most severe urinary symptoms but no physical signs were present.

The following case admirably illustrates this point. "A man of sixty-two years, with a history of periodical attacks of retention for fifteen years. On rectal examination, the prostate was found to be enlarged, but both sides equal, soft and even, and not painful. An abscess was not diagnosed, acute retention and resulting uraemia proved fatal within two weeks. An autopsy revealed a prostate of normal size with numerous small calculi, each surrounded by an abscess. (There was no evidence of Gonorrhoea in the history)."

Lydston⁶¹ describes a silent abscess in which clinical signs, leucocytosis and symptoms were all absent in an old man with a hypertrophied prostate which eventually burst into the bladder.

The differential diagnosis of the condition is not difficult. It consists mainly, in differentiating it from other suppuration in the region of the prostate, such as ischio-rectal, perianal, and pelvic abscesses. The position of the abscess, as felt per rectum, usually serves to give a clue to the diagnosis. It is important to note, however, that a peri-prostatic abscess may track into the ischio-rectal fossa, and give rise to the clinical findings of an ischio-rectal abscess. A prostatic abscess guided by Buck's fascia, may easily track into the scrotum, where it can be mistaken for a periurethral abscess (Keith).

Herman⁴² quotes a case of prostatic abscess which was diagnosed as an adenoma. Le Roy⁸¹ also cites two cases in which the diagnosis of prostatic adenoma was made.

Sarcoma of the prostate has, on one occasion been diagnosed as a prostatic abscess.

Complications

The majority of cases of prostatic abscess rupture spontaneously into the urethra—usually these have been submucosal in position, but occasionally primarily situated deep in the gland.

When spontaneous rupture into the urethra takes place, a recurrence of symptoms is likely. After several such recurrences, the pathology shows a cavity or cavities, within one or both lobes, communicating with the urethra by a sinus or sinuses.

Heiman⁴² reports the case of a man of twenty-five who developed pyæmia ending in the formation of a lung abscess and empyema.

A fatal case of staphylococcal abscess of the prostate complicated by a subdural abscess has been reported by Martin.⁶³ McCarthy⁶⁴ reports a morbidity of twenty-seven per cent amongst a hundred and four cases in which the abscess ruptured spontaneously. Obviously, therefore, spontaneous rupture cannot be considered a cure.

Cummings²⁷ details the case of a man aged sixty, whose prostate was converted into a hollow cave or pouch, apparently as the result of a prostatic abscess. The case gave rise to much difficulty in diagnosis, for cystoscopy was, at first unsuccessful, the end of the instrument becoming lodged in the pouch. A cystourethrogram eventually made the diagnosis clear, where the prostate should have been, there was a small "false" bladder. Cummings, through a suprapubic cystotomy wound removed a wedge of tissue from the shelf between the "true" and the "false" bladder, thus converting the two cavities into one reservoir.

With bladder-washes the infection abated, and the cure was satisfactorily completed.

Rupture into the rectum via a peri-prostatic abscess is not infrequent, but the opening is usually a mere slit, and in these cases, further drainage by a larger opening is invariably necessary.

In some cases the perineum swells up presenting signs of a urethral or peri-rectal abscess and at first sight, may even resemble a hernia by giving an impulse on coughing.¹³ In these cases the abscess opens on the skin.

Legueu⁵⁹ reports cases that have resulted in pelvic cellulitis, pyæmia and pulmonary complications that proved fatal.

In recent years, thanks to the early intervention of surgery, these cases are seldom fatal and although a cure, is the rule, a fistula may often result.

Treatment

A recital of some of the present-day teaching regarding the surgical treatment of prostatic abscess may prove interesting.

Livermore and Schumann favour unilateral perineal incision and blind puncture of the abscess by plunging a haemostat up through the ischio-rectal fossa

Keyes dismisses all other methods in one sentence, and then describes in detail the virtues of Stevens ⁹³ method of blind puncture per urethra with the tip of a sound Stevens ⁹³ mentions eight cases in which the abscess was successfully ruptured, in this manner

Chetwood ²⁰ and Dittel ⁴³ gave about equal prominence to the method of finger rupture through an external urethrotomy, and the method of posterior prostatotomy through a radical perineal dissection

Eisendrath, Rohnick, and Young ³⁰ unequivocally recommend radical perineal prostatotomy

These text teachings are cited merely to show the wide difference of opinion regarding a proper drainage of these abscesses

The first consideration in the treatment of any surgical condition should not be a choice between "cutting it open and cutting it out" A proper weighing up of the pros and cons of palliative treatment should be clearly and carefully reviewed A radical operation is in some cases the most urgent and necessary requirement, at the same time in several cases it is best to attempt some form of non-surgical procedure which may cure the condition or render it more suitable for operation Probably this will represent the basis of all the surgical researches of the coming era, and ultimately this type of treatment may even replace such essential operations as are performed for gall-stones, appendicitis and perforated peptic ulcers This, of course, is not quite a correct statement, for this achievement will probably only result from new light being shed on the prevention rather than the cure of disease

Swan⁹⁹ believes that except in cases of acute retention, or in those where the tenesmus or urination is unbearable, non-operative treatment is the method of choice, which ought to be tried first He suggests hot rectal irrigations given through a two-way tube every two hours, in association with frequent gentle prostatic massage

McCarthy ⁶⁴ is also of opinion that rest in bed, sedatives, heat to the symphysis and perineum, belladonna and opium suppositories associated with rectal irrigations constitute an

excellent form of either palliative or pre-operative treatment. He insists that soft rubber tubes should be used and that an enema action should never follow these irrigations

Clark²¹ recommends a ketogenic diet as part of the palliative treatment

In the case of a gonococcal infection, Harrison⁴⁰ prescribes an intravenous injection of 0.18 to 0.28 gms sulpharsenobenzine, or electrolgol 2 ccs or antityphoid vaccine

A yet unpublished method, communicated to me by my father, has been successfully tried by him in several cases of prostatic abscess due to *Bacillus Coli*. He gives 0.1, 0.2, 0.3 ccs, daily, by intravenous injections, of Antimony Potassium Tartrate. By the fourth injection, the symptoms already begin to subside. The patent 'Bayer' products, e.g., Fouadin, have been found by him, to give no better result. The sulfonamides and its various derivatives have opened up a new page in the medical treatment of sepsis. But it will remain a question whether in all cases the sulfonamides will cure without surgical help. The scope is enormous and more so as we get newer derivatives and combinations introduced to work more specifically on different infecting organisms. But the fact will remain that once pus is formed, that must be given a drainage out.

In a few cases, prostatic massage per rectum, forming an addition to either palliative or post-operative treatment, may be of considerable use. Hyntschak⁴⁷ of Germany has clearly understood the disadvantages of indiscriminate prostatic massage. A precis of his article would be interesting at this point, even though it rather tends to pass into the realm of acute prostatitis.

1 Never perform prostatic massage in cases of acute inflammation, because there is great risk of disseminating the infection via the lymphatics and blood vessels. The frequent presence of thrombophlebitis in the periprostatic venous plexus can give rise to a general blood infection.

2 Massage is contraindicated in cases of acute inflammation. He emphatically condemns the practice of trying to make the abscess burst into the urethra by prostatic massage.

3 He advises that it should be avoided in cases where the abscess has already been drained, as it may lead to re-infection or irritation.

He aims to have cured the prostatic abscess by the combined use of drainage and antibiotics.

There exists among some surgeons, the opinion that a prostatic abscess is best drained by rupturing it with a sound per urethram. This technique has been aptly criticised by Herman and Carp⁴³ who say, "if we had to choose between this operation and procrastination we would prefer the latter." Dr Cumming's²⁶ paper which has been mentioned earlier, vividly demonstrates the intraurethral destructive possibilities of prostatic abscess. It is bad surgery to aggravate that destruction, further by passing sounds. In the first place, the operator has not a true conception of the amount of injury being done, or just where it is done. It cannot be too strongly emphasized that here is a surgical entity which should be treated by sight and not by touch. The time of touch operations is rapidly passing, and, in the near future will be relegated to the limbo of surgery.

Apart from the usual radical perineal operation for prostatic abscess, a review of the literature on the subject shows that, in a few cases, other successful methods have been tried. Barringer⁷ claims to have cured fifteen cases by the following method—

The patient is placed in the lithotomy position and the perineum anaesthetised with a local anaesthetic. The left index finger is inserted into the rectum. A lumbar puncture needle is driven into the perineum and manoeuvred between the rectum and the urethra, the tip being guided by the finger in the rectum, so that it eventually comes to rest on the posterior surface of the prostate. Each lobe is then pierced and the pus drawn out.

The contraindications to this procedure are cases in which the abscess is due to a streptococcal, staphylococcal or bacillus coli infection.

It is of academical interest to note that he discovered this method, accidentally, whilst giving a perineal local anaesthetic for a carcinoma of the prostate in which an abscess had developed.

Aschner³ describes a successful operation for drainage of a chronic gonococcal abscess by using an operating cystoscope.

Greenberger and Greenberger³⁷ describe a few cases of prostatic abscess which they treated by diathermy. There is also described an operation for draining the abscess by reaching it via the rectum. This technique, even for an abscess that is definitely pointing into the rectum, is so absurd and unsurgical a procedure, that it should be entirely replaced by the perineal operation.

A method of drainage which enjoyed a brief period of popularity on the Continent and in America, can now be mentioned

The patient is given a general or a local anaesthetic. The forefinger of the left hand is inserted into the rectum. A scalpel is driven through the skin, a little antero-lateral to the anal margin. The left forefinger guides the scalpel and prevents it entering the rectum. The blade is carefully passed deeper into the perineum until it eventually comes to rest on the posterior surface of the prostate. It is then plunged sharply into the gland and rotated to the left and right, so that an adequate perforation is made for the free drainage of pus. The scalpel is then drawn out of the wound and a pair of straight artery forceps inserted into the sinus. An attempt is made to widen the sinus by forcing open the blades of the forceps. Gentle prostatic massage, per rectum, usually succeeds in emptying most of the pus from the gland. A drain is inserted deep into the wound and a large dressing applied to the perineum.

Finally there remains to be considered the radical perineal operation. The first description of this method has been accredited to Pioust and Gosset.⁷¹

The patient is anaesthetised and placed in the lithotomy position. The skin around the perineum is cleaned and isolated with sterile towels. It is advisable to pass a sound into the urethra so that the latter's position can be easily localised during operation.

(Peterson advises the introduction of a Young's retractor into the bladder in order to press the prostate against the perineum.)

The curved perirectal incision of Zuckerkhandi is employed. It is convex towards the scrotum about three inches long and an inch and a half from the anal margin. The incision is carried down to the perineal muscles. The bulb is identified in the anterior part of the wound and retracted forward.

Peterson⁶⁸ does not advise the division of the central tendon, and suggests that it should be drawn to one side of the mid-line by narrow-blade retractors. The usual procedure, however, is to divide the tendon between two artery forceps. A careful dissection is then carried between the rectum and the urethra till the posterior surface of the prostate is exposed. A longitudinal incision is made into each lobe and the pus allowed to drain away. A prostatic abscess is usually multilocular, a finger should always be inserted into the cavity and all thin septa be broken, in order to obtain complete drainage of the abscess.

A rubber drain is inserted in each lobe and the wound around the drain packed with gauze soaked in paraffin or flavine and paraffin. The tube is drawn out half an inch every day from the second

Great care must be taken not to injure the rectum or the urethra. An injury to these structures almost invariably leads to the formation of urinary or faecal fistulae.

Summary

1 It is wrong to think that prostatic abscess only occurs as a complication of gonorrhoea, it often occurs secondary to severe infection of the kidneys or bladder, or to some distal focus of infection.

2 In all cases where there is general sepsis, the slightest perineal discomfort should preclude a careful examination of the prostate.

3 It is practically impossible to diagnose some of the chronic cases of prostatic abscess. They may only be discovered during post-mortem or during an operation for prostatectomy.

4 Except in cases where the symptoms are very severe, some form of palliative treatment should always be attempted.

5 The radical perineal operation is by far the safest and best procedure for the drainage of a prostatic abscess.

Case Reports

Case 1 A patient, a painter's Labourer, aged 33, was admitted complaining of abdominal pain. A diagnosis of Renal Calculus was made, and a very successful nephrectomy performed.

Twenty-one days after the operation the patient had acute retention of urine without obvious cause. There had been no rise of temperature but the pulse rate rose. A catheter had to be passed to relieve the retention, and for the first time the urine was noticed to be a little hazy and was found to be infected with *Staphylococcus Pyogenes Aureus*. The retention persisted and necessitated catheterisation.

Four days later there was a profuse discharge of foul, stinking pus in the urine, it was thought to be due to a discharging prostatic abscess, but the prostate as felt per rectum, did not appear to be swollen. A catheter was tied in the bladder, through which repeated irrigations were carried out.

A week later, for the first time the patient complained of pain in the perineum, especially on defaecation.

An examination at this stage showed a large, boggy prostate, with a boggy swelling extending upwards into the region of the left vesicle. The prostate was explored through a transverse perineal incision and about four ounces of thick, yellowish pus were evacuated,

from the left side of the prostate. The cavity had a very thick, fibrous wall and was lined by sticky, gummy material, which was swabbed away with small gauze swabs soaked in flavine. There was no obvious connection with the bladder or the urethra. A sound passed into the urethra was outside the cavity. A tube was placed in the cavity and the rest of the wound was sewn up. The pus gave a pure culture of *staphylococcus pyogenes aureus*.

The patient still had to be catheterised for three more days and thereafter passed his water naturally. A little urine leaked through the perineal wound for a day or two. Within ten days the urine was quite clear.

He made a rapid recovery and on discharge from Hospital was very fit and was passing uninfected water. His wounds were soundly healed.

This case represents several interesting points.

1 The occurrence of a renal carbuncle and its exceedingly successful treatment.

2 "The subsequent formation of a prostatic abscess which announced its presence in a characteristic fashion, namely, by causing urinary retention and giving no rise of temperature. It was also a long time in showing itself to an examination per rectum."

3 "The rapid and complete recovery of the patient and the almost instantaneous clearing up of the urinary infection after drainage of the prostatic abscess."

Case 2 A man aged sixty-two years, was admitted complaining of acute retention for twenty-four hours. He gave a history of similar attacks about once a year for the last fifteen years. The attacks lasted two days and there was no hæmaturia or pain in micturition. He had never been catheterised, and no history of gonorrhoea was obtainable.

On examination, the bladder was palpable up to the umbilicus. Per rectum, the prostate was enlarged, both sides equal, soft and even, and not painful.

The patient's general condition was good. The temperature 97.6°F, pulse-rate 82, and respiration 20 per minute. The urine showed a heavy cloud of albumin.

He passed thirteen ounces of urine normally, on the day of admission, and thirty-six ounces on the second and third days after, but on the fourth day retention was complete, and all efforts to pass a rubber catheter failed. Metal sounds up to 8/11 were passed with difficulty.

The temperature during this period was never above 99°F and pulse-rate 88, respiration 20 per minute. Twenty-four hours later, the patient had a rigor, the temperature rose to 103°F, the pulse-rate 120, and respiration 32. The mental condition was very poor and there was incontinence of urine and faeces. This condition grew steadily worse.

On examination the urine contained albumin, blood, sugar and bile. Temperature remained always below 99°F, but the pulse-rate

increased from 88 to 130 per minute on the day death occurred (fifteen days after admission)

Autopsy revealed a bladder containing foul pus and mucus, a prostate of normal size containing many small calculi, each surrounded by an abscess. Death was due to uraemia and ascending pyelonephritis.

Case 3 A man aged forty, was admitted complaining of vomiting, pain in the left side and a general feeling of illness for the last three weeks, and with a temperature of 100° F every night.

A perinephric abscess was diagnosed, incision and drainage performed two days after admission. A persistent rise of temperature, varying between 99-102° F, led to a further exploration of the wound four weeks later.

Three weeks later, the patient complained of a sore place in the perineum. The average temperature was 99° F. Two days later there was acute retention. The patient was catheterised and thirty ounces of urine withdrawn. Great relief was immediately experienced.

Within twenty-four hours he again had acute retention. Per rectum, there was tenderness anteriorly, and a prostatic abscess was diagnosed.

An operation was decided upon. An incision was made into the anterior wall of the rectum, below the prostate. A large quantity of pus poured out, a rubber catheter was introduced and the cavity irrigated with saline. Digital examination showed the cavity to extend forwards into the perineum and upwards towards the pelvis. The terminations of both extensions could be reached with the finger. The cavity was lightly packed with gauze soaked in paraffin.

The temperature and pulse-rate rapidly fell to normal, and the patient made an uneventful recovery.

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Rational Therapeutics

THE MEDICAL TREATMENT OF HYPOMENORRHOEA & OLIGOMENORRHOEA

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Hypomenorrhoea is a type of menstrual abnormality characterised by scanty blood loss at the time of regular menstruation while in oligomenorrhoea, in addition to scanty flow, the menstrual periods are often postponed for two to three months and sometimes even longer. Both these complaints are not infrequently found among young patients who may also suffer from sterility and require treatment solely from that point of view, as the condition, otherwise, does not seem to have any deleterious effect on them. The associated obesity and the menopausal symptoms seen in elderly patients are often attributed by them to hypomenorrhoea or oligomenorrhoea but all of them are in reality the results of one common factor, the disturbed hormone or endocrine function.

Hypomenorrhoea or scanty menses must be diagnosed only after ascertaining from the patient that the actual blood loss and its duration have definitely been reduced from what she used to get previously. Some individuals have very scanty menstrual bleeding right from the time they started menstruating and that amount, being quite normal for them, does not call for any treatment, provided P. V. examination does not show hypodevelopment of genital organs. These patients still stand the chances of conception as the phenomenon of ovulation and not the quantity of blood lost at the time of menstruation governs the process of fertilisation. If, however, a patient notices a definite reduction in the amount of blood loss as compared with her previous menses it is definitely pathological and needs a thorough investigation of the case on that account. Every case should have a thorough P. V. examination to rule

out the presence of tubercular lesion of the uterine appendages, chronic pyogenic salpingo-oophoritis which has completely destroyed the function of the ovaries or the presence of an early pregnancy if hypomenorrhoea is of a very short duration not exceeding beyond two or three months. In the latter type of patient, in spite of pregnancy, there may be very slight bleeding from the uterus at the time when a normal period may be expected, had not the present conception occurred. Such cases are no doubt very rare, yet before any line of treatment is started to increase the menstrual bleeding, the presence of pregnancy must be ruled out to avoid unnecessary treatment.

In addition to the underdevelopment of the genital organs the other causative factors are the failure of ovarian function resulting from prolonged lactation, menopausal changes or operative or radium castration. The general systemic diseases, e.g., severe anaemias, vitamin deficiencies, chronic malaria, and advanced tuberculosis, etc., may debilitate the patient so severely as to bring about temporary hypofunction or stoppage of function of the ovaries. In these individuals the cessation of menstruation or scanty loss is produced as a nature's attempt to reduce the blood loss and to prevent further debility. They do not require treatment for hypomenorrhoea but rather for general debility and the primary systemic disease producing it. The associated sterility, too, needs no treatment as these patients are not in a fit physical condition to go through the strenuous ordeal of pregnancy and labour.

Thus it will be evident that the only cases which definitely require medical treatment are those in which some sort of hypodevelopment is noted in the genital organs or those cases which were treated for the primary systemic disease and are now rendered fit to have the strain of normal menstruation, pregnancy and labour. The treatment required is mainly medicinal one and it must be well realised that the often misused operation of Dilatation and Curettage is not going to increase the blood loss at the time of the menstrual period. It is, in fact, not at all indicated and its use from a therapeutic point of view should be thoroughly condemned. Incidentally it may be mentioned that the only operation which is noted to increase the blood loss and bring about slight development in the genital organs is the Cott's operation or presacral neurectomy done for relieving associated dysmenorrhoea. It

is worth the trial as it increases the blood supply of the genital organs and thus produces anatomical and functional alterations. The same changes can be brought about temporarily by a thorough course of diathermy treatment to the pelvic organs. The medicinal treatment is very similar to the one required for oligomenorrhoea and will be discussed along with it.

As stated in the beginning, oligomenorrhoea is the result of an altered rhythm in the menstrual cycle, the interval being prolonged to a variable period beyond four weeks. The condition may be brought about mainly by the changes in the ovarian cycles which may be of two types: the first is only an Atavistic condition from the functional point of view, the patient's ovary goes into a stage of cessation of activity or resting phase soon after a menstruation. This phase of dioestrus may last for a varying period at the end of which the follicular maturing and corpus luteal phases develop in the ovary and the patient gets a normal menstruation though apparently after a rather long interval. This condition from all practical point of view is normal, the only fault being that the patient stands fewer chances of conception than the normal individuals as the ovulation occurs on fewer occasions throughout the year. If an endometrial biopsy is taken a week before the expected period, one often finds a fully developed secretory phase. In second variety of oligomenorrhoea there is a disturbance of the preovulatory phase, resulting in the failure of the ovulation. There is thus produced a cystic growth of Graafian follicles which fail to undergo maturity and hence end in atresia until eventually one may proceed further in maturity and bring about menstruation. The Endometrium goes on proliferating throughout the interval and no secretory change is ever seen in it. During this period of amenorrhoea there are rhythmic rises and falls in the oestrin contents of the blood at fortnightly intervals and after two or three such falls, there occurs sudden bleeding from the proliferated endometrium. The uterine bleeding is, however, very scanty in amount and of a short duration, unlike the prolonged bleeding of Metropathia Haemorrhagica. Clinically the patient is rather an obese individual with occasional masculine distribution of hair on the abdomen and extremities. The other female sexual characters, however, may be well developed and the P V examination reveals the underdevelopment of the internal

genital organs. Moreover, these patients stand very few chances of conception as the ovulation occurs only occasionally.

It will be evident from the above discussion that the treatment of oligomenorrhoea should be instituted with a view to hurrying up of the ovarian cycles in the first type of condition described above and in the second type attempt may be made to favour ovulation and corpus luteum formation. Both of them require hormonal line of treatment and it should only be administered if the general condition of the patient is found to be fit for having menstruation at monthly interval or strong enough to go through the strain of labour as was indicated previously when dealing with the condition of hypomenorrhoea.

If the patient is found much run down in health she should be treated mainly for the associated medical cause. In addition to it, she should have general tonics, ample milk and fresh vegetables. Fresh air and change to some healthy resort may be really welcomed by the patient. She should be given plenty of vitamin A and D and in order to improve her general anaemic tendency, crude liver extract like Polivex with strong vitamin B preparation may be injected daily. Iron by mouth, in the form of Blaud's Pills with aloin, two tds after food, will deal with the secondary anaemia and also favour an increase in the menstrual flow. All these measures are meant for the patients whose health is below normal and when it is noted that hypomenorrhoea or oligomenorrhoea is the result of some systemic disease.

For individuals, who are physically quite fit but for their fatty tendency, the treatment with thyroid extract will be much beneficial. The thyroid dosage should be about a gram of desiccated thyroid gland daily to every minus ten of the basal metabolism, but this dose can be raised or lowered according to the individual's response to treatment. A rapid pulse rate, undue nervousness, palpitations are indications to reduce the daily dosage of thyroid extract. Occasionally the symptom of oligomenorrhoea or hypomenorrhoea is but part of a series of symptom complex which one groups them under the term of menopausal syndrome. Such an onset of the menopause may come on after the age of forty or in some unfortunate individuals with secondary Frohlich syndrome it may appear in the early thirties. In the latter type of patients there is usually late onset of menarche or puberty and these are the ones who

require the above mentioned treatment to increase the blood loss and regulate the ovarian function. In the elderly patients, with natural menopause, hypomenorrhoea or oligomenorrhoea does not require all the costly hormonal treatment, the small doses of oestrin being given to check the embarrassing complaints like hot flushes of the face, severe attacks of headache, palpitations, hysterical manifestations and atrophic conditions of vulva and vagina with severe itching and burning in those regions. To counteract the nervous manifestations, produced by the excessive action of the pituitary gland which is then without the usual control of the ovarian hormone, oestrin, male hormone may be used. But this will bring about complete cessation of menstruation and not increase the menstrual loss. This fact must be explained to the patient and it should be impressed on her mind that with the stoppage of menstruation she will be completely relieved of her other troubles. The regulated diet and exercise will make the life of the individual more comfortable and the use of thyroid extract will raise the basal metabolic rate and reduce her body weight.

In young individuals with prominent symptoms of sterility and hypo or oligomenorrhoea, the use of Pituitary gonadotropic hormone is definitely indicated and gives much more gratifying results than in the cases of primary amenorrhoea. The follicular maturing hormone, formerly called Prolan A, may be given during the first fortnight following a menstrual period. The hormone is available as an extract from the animal pituitary glands in the form of Prephysin or as extracted from the serum of pregnant mares in the first half of pregnancy, as Serogan or Antostab. Any one of them may be administered in the dose of 1 c c or 100 rat units, five intramuscular injections being given at the interval of four days. For the immediate production of ovulation, the follicle-maturing hormone may be given intravenously two injections being given, 80 units each. There is, however, a risk of production of shock in the sensitive individuals as the preparation contains the protein molecule to which the hormone is adsorbed. Thus there are chances of antihormone production in the patient's blood, which can explain the subsequent failure of treatment if it is required over a longer period.

At the end of the course of injections with follicle maturing hormone the lutenising hormone of chorionic origin may be

administered to the patient with a view to bringing about ovulation and the development of a corpus luteum in the ovary. The available preparations of the lutenising hormone are extracted from the urines of pregnant women at about the third or fourth month, and must be given in the form of intramuscular injection, the dose being 100 rat units, i.e., one c.c. every third day till the menstruation occurs. The chorionic gonadotropic preparations like Antuitin S, Pregnyl, Gonan or Phyllosolab may be found quite useful.

In addition to the above mentioned injections of the pituitary hormones a trial may be given to the ovarian hormones as a supplementary therapy provided the correct choice is made of the type of hormone to be used and also of the proper period during the menstrual cycle. They can be administered even by oral route as the crystalline preparations, now available, are found quite effective when given by that way. The temptation of using huge doses must be avoided as they may have inhibitory action on the function of the anterior pituitary gland, and more harm may be done thereby. Oestrin may be given in the form of 1 mgm tablets b.d. by mouth during the first fortnight following the menstrual period or two intramuscular injections of 10 mgm Ovocyclin P during the first week. This will favour the growth of the endometrium and the uterine musculature. In the second fortnight, however, the oral dose must be reduced by half. Along with it small doses of corpus luteal hormone may be given in the form of tablets, 10 mgm Lutocyclin tablets being administered daily morning and evening. At the end of the month following the previous menstrual period all the treatment is stopped till the bleeding occurs from the uterus. This is likely to be seen within a few days of the stoppage of the treatment in a favourably responding case. The same course of injections and oral treatment should be carried out during the two subsequent menstrual cycles at the end of which the normal flow and rhythm of the menstrual cycle may be expected in successful cases.

The use of low dosage irradiation of the hypophysis and the ovaries is often recommended for the treatment of oligo and hypomenorrhoea but it must be realised that this procedure is not without danger in all the cases. Since such patients also suffer very frequently from sterility, the exposure of the ovaries to x-rays may injure the germ plasma and reduce still

further the hopes of conception Geller irradiated animal ovaries with increasing doses and stated that the first change that could be demonstrated histologically was a destructive one. These findings are no doubt accurate but a mass of evidence has appeared favouring the theory that the doses of radiation too small to produce demonstrable organic changes have a definite effect on the glandular function. The more convincing reports are those of Thalar who reported a series of 147 cases suffering from various types of menstrual dysfunctions treated with one-third the castration dose. 40 out of 60 cases of primary and secondary amenorrhoea and oligomenorrhoea were cured and several pregnancies occurred in women who had been sterile before the treatment was instituted. But it is quite evident from all the reported series of clinical cases, that a large number of failures are noted along with the successes. This indicates the importance of proper selection of cases for mild roengen therapy. The treatment should be carried out by a competent radiologist, the dose being not exceeded beyond 150 r to the ovaries using the roentgen rays in the treatment of young women in whom the capacity of conception is still to be preserved. If the precautions mentioned are observed during the mild irradiation therapy irrecoverable damage to so vital an organ as the pituitary or the ovary can be avoided.

Critical Notes and Abstracts

HINE'S COLD PRESSURE TEST

This test is a clinical test and it is devised to determine the reactivity of the blood-pressure. It measures the reaction of the blood-pressure to a standard stimulus.

The test is performed with the subject supine. If other positions are used, the effect of posture, sitting or standing, must be taken into account in evaluating the results. The nature of the test is explained to the patient to minimize apprehension. The patient should not have taken drugs which cause vasodilatation or sedative for at least twenty-four hours, prior to the test. Slowly excreted drugs like the bromides may affect the response longer than twenty-four hours. The temperature of the water should not be more than one degree above or below 4°C , and it should be measured just before the hand is plunged into it.

The subject rests supine in a quiet room and is given rest for twenty to sixty minutes. Several readings of blood-pressure are taken until an approximately *basal level* has been reached. With the subject still supine and with the cuff of the sphygmomanometer on one arm, the hand on the opposite side is immersed in ice water (4°C) to a line just above the wrist. With the hand still in the water, readings of blood-pressure are taken at the end of *thirty* and of *sixty seconds*. The highest of the two readings obtained while the hand is in the ice water is taken as an index of the response. The hand is removed from the ice water as soon as the reading at sixty seconds has been made and readings are taken every *two minutes* thereafter, until the blood-pressure has reached to its previous basal level.

The maximal response frequently occurs with thirty seconds. The blood-pressure returns to the basal level within two minutes after the hand is removed from the ice water, in subjects with usually normal pressure, while in the presence of established hypertension, return of the blood-pressure to the basal level may be delayed.

The diastolic response to the stimulus is a more reliable index of vasoconstriction than the systolic response, but it is advisable to record both readings. Analysis of the results of a large number of tests has determined that *an elevation, above the basal level of more than 20 mm of mercury in systolic pressure, and of more than 15 mm of mercury in diastolic pressure indicates a hyperreactive response to the stimulus*.

Range of variations at repeated examinations is very slight, and the response in the same individuals is remarkably constant. Hines has performed the test some 5,000 times in 1856 persons and has

divided his subjects into (1) Persons with normal basal levels—(a) hyporeactors (when the elevation in blood-pressure is less than 20 mm in systolic and less than 15 mm in diastolic reading), (b) hyperreactors (when the rise in blood-pressure is more than 20 mm in systolic and more than 15 mm in diastolic reading) Of his cases 85 per cent were hyporeactors and 15 per cent were hyperreactors (2) Persons with basal essential hypertension show the mean response from two to six times greater than that of the subjects with usually normal blood-pressure, i.e., the elevation is 40 to 120 mm in systolic and 30 to 60 mm in diastolic reading

The test is useful in detecting (1) cases of *latent* hypertension, (2) cases of essential hypertension in whom the basal level is low at the time of examination because of coronary lesion or congestive cardiac failure, and (3) cases in pre-hypertensive state—candidates for essential hypertension

The test may well be used in determining the hereditary factor in essential hypertension Hines from an examination of a limited number of cases suggests that the hypertensive trait—a vasomotor system which reacts excessively to certain external and internal stimuli and eventually produces a state of essential hypertension—is inherited as a dominant characteristic A hyperactor has at least one parent who has essential hypertension or gives a hyperreactive response to cold pressure test

N D P

FLUCTUATIONS OF BLOOD PRESSURE

Blood-pressure is not static but labile Several blood-pressure readings should be taken at hourly intervals and maximal, minimal and the rough average blood-pressure should be recorded and not a single isolated blood-pressure reading

The systemic blood-pressure may show variations from 15 to 65 mm of mercury and a mean variation of 36 mm Hines and Brown's ice water test is a clinical device for measuring this variability of the blood-pressure The majority of subjects with normal blood-pressure have a range of variability of 10 to 20 mm of mercury in systolic and diastolic pressures About 15 per cent of persons with a normal pressure have a marked variability of two to three times greater than the mean change in the normal reactions, and these subjects are called normal hyperreactors

The systolic and diastolic pressures may fluctuate dissimilarly The systolic pressure may show a considerable rise, while the diastolic pressure may show little or no change But when there is a marked change in the diastolic pressure, there is usually a similar change in the systolic reading *The diastolic response is the more reliable index of vasoconstriction* The changes in the systolic pressure alone such as occur in hyperthyroidism and the effort syndrome, are largely the result of increased cardiac output rather than vasoconstriction

Unusual fluctuations of the blood-pressure in subjects with normal blood-pressure are indicative of a pre-hypertensive state,

The normal range of systolic blood-pressure is between 90 and 120 mm and the normal range of diastolic pressure is between 60 and 80 mm of mercury. Any elevation of diastolic reading, however transitory, and an unusual response of the diastolic blood-pressure (more than 15 mm of Hg in cold pressure test) seem to be of special significance. Such persons are most likely to develop hypertension in later years.

Essential Hypertension

The blood-pressure of patients who have essential hypertension varies widely. This fact must always be kept in mind in evaluating any therapeutic measure. Clinical experience indicates that the probability of influencing the blood-pressure satisfactorily by any therapeutic procedure is roughly proportional to its tendency to approach normal as a result of rest, sleep, sedation or anaesthesia. To get a basal reading, two doses of three grains of sodium amytal should be given at hourly intervals, and the blood-pressure measured at the end of the third hour. There are rarely any symptoms associated with fluctuations of blood-pressure in cases of essential hypertension, in contrast to paroxysmal hypertension associated with Chromaffin tumours, in which the changes in blood-pressure are associated with symptoms. The ceiling beyond which pressure will not go, as a result of external stimuli, *e.g.*, in cold pressure test, is usually about 250 mm for the systolic pressure and 150 mm for the diastolic pressure.

Paroxysmal Hypertension

Phenochromocytomas, of which about two-thirds are in the suprarenal glands, affect individuals from 16 to 69 years of age and cause paroxysms of hypertension as often as several times daily, lasting for one or two hours or for only two or three minutes. Paroxysms occur spontaneously or are induced by physical exertion, sneezing, body bending, or pressure on the abdomen, and are associated with (1) palpitation, (2) pain, precordial, epigastric or in the head, (3) vomiting, (4) rapid respiration, and (5) sweating. The face becomes pallid or cyanosed, neck veins may become distended, there are no convulsions, chill or fever, the blood-pressure is increased and there may be wave-like variations, the pulse-rate may increase, decrease or may not change, there is a palpable abdominal tumour in half of the cases and positive roentgenologic findings in about two-thirds of the cases. Hyperglycaemia and glycosuria may occur during the paroxysms.

Orthostatic Hypotension

In orthostatic hypotension the blood-pressure decreases on assuming erect position instead of rising as occurs ordinarily. It is associated with weakness on getting up, deficient sweating, failure of pulse-rate to increase normally on assuming erect posture, accentuation of symptoms in warm weather and excretion of larger amount of urine when the patient is recumbent than when he is erect.

Miscellaneous

Holding one's breath, grunting, pain, fever, excitement, anger, muscular effort, insomnia, episodes of angina pectoris, lymphosarcoma of the superior mediastrium, carcinoma of larynx, or oesophagus, meningitis tobacco smoking,—each of these may cause marked increase and fluctuations in blood-pressure. The blood-pressure is higher in the leg than it is in the arm. When it is not, coarctation of the aorta should be suspected. Blood-pressure is unequal in two arms in about half the normal persons. The inequality is about 13 mm of mercury and it is not constant but transient. If it is marked and persistent, one should suspect local organic disease.

(Hines and Allen Modern Concepts of Cardiovascular Disease,
8 No 11, Nov 1939)

N D P

Book Reviews and Notices

INJURIES OF THE SKULL, BRAIN, AND SPINAL CORD, Neuro-psychiatric, Surgical and Medico-legal Aspects Edited by Samuel Brock, written by twenty-two different contributors Published by Williams and Wilkins, Baltimore, pp 632, price Rs 32/-

There was a real need for a book of this size and scope treating injuries of the central nervous system in sufficient detail to be of practical use. This comprehensive work is carefully designed to meet the requirements of general practitioners, neurologists, surgeons, radiologists, psychiatrists, lawyers, judges, and insurance officials. Even pediatrics and obstetrics are represented in chapters on Cerebral Birth Injuries and Birth Injuries of the Spinal Cord. Only the injuries of the Peripheral Nerves are not discussed. Except C P Symonds of the Guy's Hospital, London, who writes on Concussion and Contusion of the Brain and W Ritchie Russel of Edinburgh who contributes a chapter on Injury to Cranial Nerves including the Optic Nerves and Chiasma, all the contributors are American. All are recognised authorities on their subjects and have actually written, as the editor says, a series of comprehensive monographs on neurology, psychiatry, neuro-surgery (in its civil and military aspects), radiology and forensic medicine as far as these subjects relate to injuries of the skull, brain, and the spinal cord. The problems of the injury to the nervous system are many. There is no agreement about the immediate and late physiological and pathological changes as a result of trauma. The different views are presented here critically, much new ground is covered, and though there is some overlapping and confusion in the use of some terms such as concussion and contusion, the editor has tried to minimise these by explanatory notes and cross references. We have nothing but whole-hearted praise for the production and we feel sure it will be welcome to all lovers of progressive scientific medicine, and all will profit by it. We draw the attention of the readers to the excellent clinical descriptions of concussion and contusion (where the teachings of Wilfrid Trotter are clearly presented), Massive intracranial haemorrhage of traumatic origin, Chronic subdural haematomas of infants (a condition largely overlooked), Chronic subdural haematomas in adults (a condition more common than thought of and again made familiar by the writings of W Trotter), Subdural hydroma, Post-traumatic convulsive and allied states, Post-traumatic neuroses and psychoses, Sprains and strains of the spinal cord, Circumscribed serous spinal meningitis, Herniation of the nucleus pulposus after injury, and various syndromes produced by injuries of the spinal cord and nerve roots. Most chapters contain complete case reports and well produced histological and radiological illustrations. The chapter on the

Medico-legal aspects is complete in all respects, has as many as 408 references, and is a veritable mine of information on all problems a physician is likely to meet, not only in neurological but in general medical practice

DIETETICS IN GENERAL PRACTICE by J R Goyal, MBBS, published by The Medical News, P O Box, 81, Delhi, 1943 pp 94+76, price Rs 8/-

In this booklet, Dr Goyal has attempted to summarise modern knowledge about the importance of diet in health and in disease. The first part deals with the principles of dietetics and in the second part applied dietetics are discussed from the general practitioners' point of view. The author has kept the Indian conditions in mind and has given the composition of cereals and other articles of diet commonly used in India. One feels that a little more detailed information and instruction would have been welcome to the general practitioner in planning his diets in various diseases. Even in these hard times of war and the mismanagement of the paper industry by the Government it appears to us that the price of rupees eight for a pamphlet of some 175 pages is rather exorbitant and the book will fail to reach the general practitioner for whom it is meant.

YOUNG OFFENDERS—An enquiry into Juvenile Delinquency by A M Cari Saunders, Herrmann Mannheim and E C Rhodes, published by The Cambridge University Press, 1942, pp 168, price 7s 6d

That a country in the midst of a total war and at a time when its very life is threatened can institute such an enquiry, carry it on in the midst of terrible bombardment and publish its report, shows the tenacity of the British mind and the soundness of the British social conscience. Juvenile Delinquency is akin to Crime in adults and its roots are not in the innate badness of the child but in his social environment. The advent of the cinema, the motor vehicle, the wireless, the newspaper and the organised sport are the new circumstances of modern urban life to which the child is exposed. The parental relationship is another factor in juvenile crime. Abnormal families, broken homes, prolonged friction between parents, all predispose children towards delinquency. Out of 47 homes where the heads, not being parent of the case, were cohabiting, 43 had cases of delinquency. Even in homes of normal structure the attitude of either parent towards the child, harshness or indulgence, or alternately both, and laxity in discipline in allowing the child to be out after dark appear to be the potent factors and so is unemployment, absence from school or work, affording opportunity for mischief. Why some children are susceptible to such abnormal circumstances and not others is a psychological problem and is not touched by this enquiry. Juvenile crime is on the increase in all urban areas and such enquiries are necessary if we are to devise effective preventive measures. The methods adopted by these objective workers should be a model for others and we recommend this summary of a detailed

report, which is to be published later, to our social workers, magistrates and physicians who have to deal with child crime

THE DOCTOR AND THE DIFFICULT CHILD by William Moodie, MD, FRCP, DPM, Medical Director, London Child Guidance Clinic and Training Centre. Published by Humphrey Milford, Oxford University Press, London, 1941, pp 214, no index, price \$1 50

This is a well-written little book which will be welcome to physicians, parents and school teachers. It is a practical book, not a scientific treatise, written by a practising physician from a rich clinical experience. The book is made up of two parts, the first part deals with the Recognition, Study and Treatment of the Problem and the second part contains 18 common problems of child behaviour clinically described and studied. These symptoms are Stealing, Lies, Fancies, and dreams, Feeding difficulties, Unmanageableness, Backwardness, Nervousness, Nervous movements, Enuresis, Violent behaviour, Sex difficulties, Truancy and wandering, Lack of concentration, Speech defects, Fits and seizures, Psychosis in children, Anxiety, Disturbance of sleep, and Mental deficiency.

Dr Moodie writes in a simple unaffected style and does not encumber his thesis with technical jargon and odd theories as is the case with most writers on psychological medicine. He does not uphold any particular school of medical psychology but often drives home his point by saying,—“clinical experience proves that this is a fact.” He gives a number of case histories to illustrate his argument. Most of the child's difficulties arise from failure to get satisfaction of his imperative emotional needs for *work, security, and affection*. At the same time he does not minimise the importance of physical illness, mental defect, or dietetic errors as a possible source or contributing factor in disturbances of behaviour and personality. No physician, parent, or school teacher will fail to derive benefit from the perusal of this informal discussion, as the author prefers to call this clinical manual.

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- 1 THE INDIAN PHYSICIAN 1942 Vol I Nos 1 to 12, a few
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- 2 THE PREVENTION OF DIABETES MELLITUS
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THE POPULAR BOOK DEPOT, Lamington Road, Bombay 4

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— asks Shakespeare To the medical profession a name, or rather a good name, is of paramount importance — only to be achieved by years of meritorious service and maintained by meticulous observance of scientific method and professional etiquette, and the same strict and rigid standards are applied to the manifold products used in the art of healing. Thus to obtain acceptance by the medical profession, the manufacturer of drugs and biological products has to prove his integrity of purpose and strict adherence to scientific method over a long period. Standard Pharmaceutical Works may now claim to have joined the small band of manufacturers whose name to a product is accepted without question as being sufficient guarantee of its efficacy and quality. We specialize in injectibles and biological products. Every product is backed by years of patient research, meticulous attention to detail and experience in the manufacture of sera and vaccines and injectable products under tropical conditions.



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VOL II NO 4

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WHOLE NO 16

Original Contributions

WEIL'S DISEASE OR LEPTOSPIROSIS IN BOMBAY

A REPORT OF SEVEN CASES

By

V. V. SHAH

M.D., (BOM)*

From Bai Yamunabai L. Nair Charitable Hospital

BOMBAY

A number of patients suffering from fever followed by jaundice are being seen in the hospital and private practice, but all such cases when they recover are often stamped as suffering from catarrhal jaundice and when they die as infective jaundice without laboratory confirmation. The object, therefore, in presenting this note is two-fold (1) to show that leptospiral infection is commoner than what is being supposed and (2) to present clinical features in order to facilitate its recognition so that a case of leptospirosis may not be missed.

My interest in this disease was aroused by the sudden appearance of a crop of jaundiced patients in the latter part of September and beginning of October 1942 at the Bai Yamunabai L. Nair Charitable Hospital, Bombay. Out of these only a few could be admitted in the hospital while others did not consent to get admitted. Most of those patients, who were admitted, could be established as suffering from leptospirosis after proper laboratory investigations.

A survey of the literature shows that a number of case reports with clinical signs suggestive of leptospiral infection (Tucker 1907, Parmanand 1922, Turkhud 1928, Manohar 1940) have been made but the laboratory confirmation was la-

in all these cases More recently Lahiri (1941) reported a case of leptospirosis from whom the causative organism was isolated

Case Reports —

Case 1 A Muslim male aged 20, occupation, sweeper, residence, Kamatipura was admitted on 26th September 42 for diarrhoea about 30-40 stools per day with frank blood in the stools for last 7 days History of fever, severe bodyache and headache for last 8 days On examination T 96° F, P 98 per minute, R 28 per minute, deep jaundice, anaemic conjunctiva markedly congested Liver +, Spleen +, Temp normal after admission Urine, bile salts and pigt present Stools Blood present, no pus cells or macrophages Van den Bergh—immediate direct positive RBC—384 mil Hb—70% CI9 WBC 8400 P 69, L 29, E1, LM1, Vacuolation of RBC with poikilocytosis Agglutination test —1320 positive against classical strains

Case 2 A Hindu male aged 25, occupation—panwalla, residence Kamatipura was admitted on 23-9-42 for continuous fever and severe aching of calf muscles for last 4 days On exam Temp 101.5°F pulse 106 per min respiration 26 per min Prostration present, congested eyes, noticed jaundice on the 5th day of the disease Liver and spleen not palpable, Tem normal on the 12th day of disease Patient had after-fever on the 16th day of disease continuing for 8 days Urine Alb trace, Bile salts and pig present Van den Bergh—immediate direct positive, WBC 9200 per cmm P 84, L14, H1, E1 Blood culture —organisms grown, Urine—Inoculation into guinea-pig-organisms isolated Agglutination test —positive final titre being 1 100,000

Case 3 A Hindu male aged 25, worker in an ice factory, Lamington Road, was admitted on 15th September, 42 for fever-rigors, headache, bodyache and marked aching of calves for last 4 days Temp 100.6°F, pulse 110 per min, respiration 26 per min, great prostration, markedly congested conjunctiva, deep jaundice, liver +, spleen +, Urine, alb nil, bile salts and pig present, Van den Bergh—immediate direct positive WBC 7,600 per cmm P 68, L 30, H 2, E nil Urine—organisms isolated after inoculation into guinea pig Agglutination test—positive 1 100,000 final titre

Case 4 A Hindu male aged 20, occupation milkman, residence, Kamatipura, was admitted on 2nd October 1942, for fever, headache, bodyache and marked aching of calves for the last 6 days Temp 99.6°F, pulse 100 per min, resp 26 per min Prostration present, conjunctiva congested, jaundice nil, spleen + Urine—Bile salts and pigment nil Agglutination test positive 1 1280 Temp normal, on the 8th day of disease

While going through the records of the hospital, it was found that three cases of leptospirosis (refer table below) in which the diagnosis was confirmed by laboratory investigations, were also treated in the months of August and October 1941 The details of the

clinical picture of four cases only have been given as I had occasion to watch them personally from day-to-day

TABLE

Serial case number	Date of admission	Occupation	Part of Bombay in which he is residing	Blood culture	Isolation of organisms after inoculation into Guinea pigs	Aggl test
1	26 9-42	Sweeper	Sankli St 1st Lane, Kamatipura			positive 1 320
2	21 9-42	Panwalla	Kamatipura 2nd Lane	Organisms grown	Isolated	positive 1 100,000
3	15 9 42	Worker in Ice factory	Imperial Ice Factory, Larington Rd Bombay		Isolated	Positive 1 100 000
4	2 10-42	Milk man	Kamatipura 4th Lane			Positive 1 1,280
5	22 8 41	Moulder	Kamatipura 15th Lane	Negative	Isolated	Positive more than 1 100,000
6	3 10-41	Restaurant keeper	Dhobi Talao		Isolated	Positive more than 1 100,000
7	2 10-41	Hotel servant	Dongri Jail Road			Positive 1 100 000

In the case reports given above and as shown in the table, it is interesting to find that out of the seven cases of leptospirosis, four came from different lanes of Kamatipura and one from an area nearby Kamatipura and that all the cases occurred in the months of August, September and October (latter part of monsoon) It can also be seen that some of the clinical features like aching of the calves and conjunctival injection were very constant. There were no haemorrhages in the skin noted and only one patient had bleeding per rectum associated with frequent diarrhoeic stools. This patient could easily be mistaken as suffering from dysentery and especially bacillary type in view of the associated fever and toxæmia unless a proper examination of stools was made. It is interesting to note that case No 4 had no apparent jaundice and his urine did not contain any bile. Albuminuria was not constant. Leucocytic count was found a little higher than normal and was not characteristic so as to help in diagnosis.

Diagnosis

While going through the case reports of leptospirosis in India and outside it is found that the clinical features are vary-

ing in degree depending upon the severity of infection. There are mild cases which even throughout the whole course of the disease do not develop jaundice and barring fever and other concomitant symptoms like body-ache, headache, etc., there may not be any signs or symptoms which may even make one suspect leptospiral infection. The diagnosis, in such cases, is very difficult and could only be made by laboratory investigations if systematically carried out in the monsoon season when infection is common or when an epidemic is going on. Apart from this most of the cases present symptoms and signs which are very suggestive of leptospiral infection. The clinical features which attracted the attention most in the cases given here were jaundice, conjunctival injection and aching of calves associated with prostration. It should therefore be known that any patient coming especially in the monsoon season, with fever, prostration, aching of the calves, conjunctival injection, with or without jaundice, should always be suspected of leptospirosis and the diagnosis confirmed by laboratory investigations.

Summary

Seven cases of leptospirosis from the Bai Yamunabai L Nair Charitable Hospital are reported. Most of the cases came from Kamatipura and all of them occurred in the latter half of monsoon. It has also been emphasized that the clinical features of leptospiral infection are such as to suggest the diagnosis which should be confirmed by laboratory findings.

I am very much obliged to Dr H V Tilak, the Chief Medical Officer, Bai Yamunabai L Nair Charitable Hospital for permitting me to go through the records of the hospital and publish these cases and also to the Hon Physicians Drs D H Dudha and P P Soonawalla under whose care, the patients were in the Hospital. All credit for the laboratory investigations goes to Dr M N Ishiri of the Haffekine Institute, Bombay, and my thanks are due to him.

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LIVER FUNCTION AND BLOOD ASCORBIC ACID IN SYPHILITIC WOMEN BEFORE AND AFTER PARTURITION

By
K D LAHIRI

M B, B S

From The Department of Skin & Venereal Diseases
Patna Medical College Hospital

PATNA

Literature

Syphilitic women are treated on lines identical with those applicable to males and pregnancy does not usually present any great difficulty except that one should be careful for the liver and kidneys. A question which is generally discussed whether every pregnant woman with a history of syphilis should be treated during pregnancy but now the consensus of opinion is that whatever the age of infection, the woman should certainly be treated but in cases in which the mother has previously received a large amount of treatment and the blood Wassermann has been negative even then one course of antisyphilitic therapy during pregnancy is very essential. Colonel Harter (1931) strongly advocates this by remarking "My own evidence in favour of treating every case, no matter how strong, is the evidence that her disease has been eradicated." (1941) advocates that a pregnant syphilitic woman should be treated during pregnancy regardless of the results of the Wassermann test. Whipple and Dunham (1938) also advocate antisyphilitic therapy for every syphilitic woman during each pregnancy.

Although the liver undergoes much strain during pregnancy, there is plenty of vitamin-C in the blood which is available to the growing fetus. It has been found by Lahiri (1941) that the liver function is not much impaired during pregnancy. Lahiri and Rudra (1942) have shown that the blood ascorbic acid is at a higher level during pregnancy and puerperium than normal. Sadowsky (1931) has examined the normal blood vitamin-C content and found the average concentration of vitamin-C to be 0.13 mgm per 100 c.c. blood.

Vitamin-C in mgm per 100 c.c. blood	
0.16	0.24
0.21	0.21
0.14	0.21
0.13	0.26
0.20	0.30
0.13	0.24
0.14	0.30
0.10	0.32
0.15	0.15
0.20	0.20
0.18	0.18

mgm per cent He also found out that vitamin-C concentration of the blood was highest during pregnancy and the average of 207 patients was 1.09 mgm per cent and after confinement it was lowest and the average of 62 patients was 0.78 per cent Yamamura and Miyaska (1940) have found in 50 pregnant women and in 22 puerperal women that the blood ascorbic acid level is below 0.5 mgm per cent Bundsen et al (1941) think that among the various substances possessing detoxifying properties vitamin-C stands in a unique position While most other substances are products foreign to the body ascorbic acid is one of the powerful physiologic detoxifying agents Prasad (1942) served that the rationale of specific corrective hepatic therapy may be said to be effective in two ways, viz, (1) by saturating the liver cells with glycogen and (2) by providing substances to the liver cells for detoxication by conjugation, oxidation or reduction process Irgang (1937) thinks that pregnancy, infection and syphilis are capable of destroying liver

ction is estimated by the hippuric acid excretion test dose of sodium benzoate Lahiri (1942)

Quick's (1931) method by giving to the bladder After 4 hours the subject and the hippuric acid excreted in this should be noted The volume of urine is brought adding water if the sample is less and if more by over water-bath and cooling down to the room 5 cc of concentrated hydrochloric acid is gently stirred for about 5 minutes and allowed to stand for

This is filtered through the Buchner's funnel over which has previously been weighed with a beaker together with the filter is kept over night to it is weighed The difference in weights gives recovered and by adding 0.5 gives in gm the excreted in the sample of urine Lahiri (1942) age excretion is 5.0 gm in normal subject lowered in women but improved within as found the liver

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Blood vitamin-C has been found out by Van Eekellen et al (1933) by the method of Tillman and Szet-Gyorgi by titrating against 2.6 dichlorophenolindophenol after treating the blood with trichloroacetic acid and found 0.5 mgm vitamin-C per 100 c.c. blood in 16 subjects. Taylor et al (1936) found the average blood ascorbic acid level in normal subjects to be 1.61 mgm per 100 c.c. Modified method of Lahiri and Rudra (1943) by mixing 2.5 c.c. of venous blood with a solution containing 5 c.c. distilled water and 2.5 c.c. of 20 p.c. trichloroacetic acid and filtering it by keeping the test tube in ice water and titrating the filtrate from a micro burette with 2.6 dichlorophenolindophenol keeping in ice water and completing the whole experiment within 30 minutes. Blood vitamin-C in normal women has been found by Lahiri (1942) to be 0.72 mgm per cent and Lahiri (1942) has found it to be reduced in syphilitics.

TABLE I

Liver function and blood ascorbic acid content in 13 syphilitic women (Positive blood Wassermann) estimated during the last month of pregnancy

Subject	Community Sex	Age	Hipp. acid in gm excreted in urine	Vit. C in mgm per 100 c.c. blood
	H.M.	24	1.47	0.27
	M.F.	38	1.84	0.44
	H.F.	42	2.00	0.34
	H.F.	41	1.65	0.36
	I Chr F	37	2.24	0.30
	H.F.	43	2.20	0.25
	H.F.	35	1.68	0.48
	H.F.	34	1.42	0.46
	M.F.	18	1.85	0.48
	M.F.	27	1.02	0.32
	H.F.	38	1.09	0.58
	F	47	2.48	0.54
		22	2.62	0.42

TABLE II

Liver function and blood ascorbic acid has been investigated in 15 syphilitic women within parturition

Subject	Community Sex	Age	Hipp. acid in gm excreted in urine	Vit. C in mgm per 100 c.c. blood
1 P.D.	H.M.	24	1.49	0.16
2 M.D.	M.F.	38	1.02	0.24
3 R.	H.F.	42	2.20	0.21
4 S.	H.F.	41	1.04	0.14
5 S.N.	I Chr F	37	2.40	0.21
6 B.N.	H.F.	43	2.24	0.13
7 J.N.	H.F.	35	1.88	0.26
8 L.D.	H.F.	34	1.53	0.30
9 N.F.	M.F.	30	2.00	0.13
10 M.B.	I Chr F	42	2.14	0.24
11 H.T.	I Chr F	30	3.45	0.30
12 S.F.D.	H.F.	30	3.10	0.32
13 R.	M.F.	32	2.41	0.15
14 S.D.	M.F.	40	1.87	0.20
15 K.D.	H.F.	40	1.94	0.18

TABLE III

Liver function and blood ascorbic acid content in 11 syphilitic women, 6 months after parturition

No	Subject	Hipp. acid in gm excreted in urine	Vit. C. in mgm per 100 c.c. blood	Antisyphilitic therapy
1	P.D.	2.20	0.39	With
2	M.B.	2.21	0.24	Do
3	H.	2.87	0.40	Do
4	S.	2.00	0.20	Without
5	S.S.	2.86	0.39	Do
6	J.P.	2.00	0.48	Do
7	K.G.	0.82	0.68	With, also had ascorbic acid by mouth
8	P.H.S.	4.00	0.62	Do
9	D.K.S.	4.04	0.65	Do
10	H.C.S.	1.21	0.64	Do
11	M.M.K.	2.20	0.34	With

TABLE IV

Comparison of different groups of cases of syphilitic women before and with syphilotherapy

During last month of pregnancy	Within one week after parturition	Six months after parturition	Hipp. Acid in gm excreted in urine	Ascorbic acid in mgm per 100 c.c. blood
13	—	—	1.09 to 2.62	0.27 to 0.58
—	15	—	1.04 to 3.45	0.13 to 0.32
—	—	11	2.00 to 4.21	0.20 to 0.65

Observation

Liver function and blood ascorbic acid have been investigated in 13 syphilitic women during the last two weeks of pregnancy (Table I). Liver function and blood ascorbic acid have been investigated in 15 syphilitic women within one week after delivery (Table II). In 11 syphilitic women the same has been done 6 months after confinement (Table III). Comparison of cases (Table IV.)

Conclusion

The average excretion of hippuric acid by Quick's test has been found in normal Indians by Lahiri (1942) to be 5.0 gm. The average blood vitamin-C content in normal women has been found by Lahiri (1943) to be 0.72 mgm. and in a mixed group of men and women Lahiri (1943) has found the blood ascorbic acid to be 1.2 mgm. per cent. Lahiri and Rupa (1943) have found the blood ascorbic acid during pregnancy in non-syphilitic women to be 0.9 and 0.5 per cent. Lahiri (1943) has found the liver function in syphilitic pregnant and puerperal women, the excretion being only 3.0 and 4.0 gm. per cent. Lahiri has found the liver function normal in syphilitics and Lal

particularly lowered in syphilitics developing arsenal intolerance. Liver function and blood vitamin-C have been found by Lahiri (1942) to improve by the administration of liver extract and ascorbic acid by injections.

It is always essential to treat every syphilitic woman at whatever stage she comes under observation but the liver function test and blood vitamin-C blood estimation should be done as a routine measure to avoid any intoxication during anti-syphilitic therapy with arsenic. The administration of few liver extract injections where the liver function is very low and few ascorbic acid injections where the blood vitamin-C content is low should always be done before starting the anti-syphilitic therapy, to avoid also pregnancy toxæmias. Peckham (1941) observed after treating 13,742 pregnant syphilitic women that antisyphilitic treatment administered to pregnant syphilitic women during pregnancy does not increase the incidence of toxæmias of pregnancy.

I am grateful to Principal Dr T N Banerjee and Superintendent, Dr B P Varma for allowing me to carry on the present research. I am thankful to Major D Murdoch, Professor of Obst for permitting me to do my experiments on some of the cases in the Hospital for Women to Mrs O K. Madhavan of the Women Venereal Clinic and to Dr T N Seth, Professor of Medical Chemistry for giving me facilities to work in the Research Laboratory, and to Mr M N Rudra for guiding the work. For help, encouragement and criticism of the work I am thankful to my Chief, Dr H P Lall and Professor B N Prasad.

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ally by Marchand. At the present time it is disputed as to whether this type could be regarded as a new growth or only as an exaggeration of the normal reaction of pregnancy. In this type there is invasion of the uterine musculature by syncytial masses surrounded by blood, fibrin, and necrotic tissue, metastases do not occur. Clinically this type has a favourable prognosis and cure following simple curettage has been frequently reported.

Syncytioma described by Ewing has been recognised by subsequent writers as a typical new growth in which there is extensive invasion of the uterine muscle by the syncytium. Ewing regarded it more as a regressive type of chorio-carcinoma, but others considered it as a new growth in which Langhan's cells had disappeared. Clinically, this variety has a benign course, but occasional fatal result occurs as a result of haemoperitonium and severe anaemia due to the erosion of blood vessels by the rapidly growing syncytium.

Novak, in 1922, suggested the classification of chorionic epithelial growth into (1) benign chorioma corresponding to benign hydatidiform mole, and (2) malignant chorioma which included the 'malignant mole' of Ewing. He considered 'malignant mole' as an essentially malignant new growth differing from the typical malignant chorionepithelioma in the degree of malignancy. He argued that it was confusing to classify 'malignant mole' as a separate group of chorioma as 'malignant mole' metastasised, recurred, infiltrated and killed just as a typical chorionepithelioma.

Clinical characters. A careful history is important in correctly diagnosing a case, as otherwise irregular attacks of vaginal bleeding may lead to errors in diagnosis. It must, however, be noted that sometimes medical advice is sought for symptoms due to metastatic growths.

As this tumour is preceded by conception, a history of recent or long past pregnancy is always obtained. The period of latency is of interest. In the case reported by Gill in 1926, the tumour occurred during the fifth month of pregnancy with a foetus. Pick has reported a case in which it had occurred three days before a mole was expelled. Walthard has reported its occurrence in a woman in her eighth month of pregnancy. On

the other hand, Geist mentioned that the period of latency as long as nine months had been reported

Age In the series of 188 cases reported by Teacher, the youngest patient was aged 17 and the oldest 55, the average age being 33 years Age does not seem to have any important bearing from the clinical point of view

Parity In the series of 188 cases reported by Teacher the fertility was as follows, First pregnancy, 477 p c, after first pregnancy, 1537 p c, after the second and third, 2824 p c, after four or more pregnancies, 378 p c From this as well as other series it appeared that chorionepithelioma occurred more frequently as parity rate increased

Vaginal bleeding is the chief symptom directing attention to this condition When the period between a pregnancy and the development of chorionepithelioma is short, a history of blood stained discharge with intermittent profuse bleeding since the expulsion of the ovum is obtained On the other hand, when the period of latency has been long, one or several regular menstrual periods may have occurred before irregular vaginal bleeding commenced As the period of latency is generally between a few months and two years irregular attacks of profuse bleeding should be investigated at their onset to exclude this condition In such cases, curettage may be performed, and whenever the histological diagnosis is 'the remains of the products of conception', the clinician should watch the patient for at least two years more Cases have been described in which the histological diagnosis was 'remains of the products of conception', and in whom chorionepithelioma subsequently developed A case reported by Novak is particularly interesting from this point of view The Aschheim-Zondek test in such cases should be the rule, four to six weeks after the curettage, to exclude the persistence of chorionic tissue

On vaginal examination the uterus may be found enlarged, but it is not unusual for chorionepithelioma to be present with a uterus of normal size The surface of the uterus is generally regular In some cases bilateral cystic tumours may be present The ovarian cysts may exceed the size of a foetal head at term They were present in 12 of the 15 cases reported by Naguib Pasha Mehfoz in 1940 Enlarged cystic ovaries were not present in any one of the three cases reported in this paper,

Secondary metastases, when present in the vulva or in the vagina, appear as raised globular or oval nodules, reddish brown in colour, and of a firm consistency. The presence of secondary nodules readily directs attention to the primary site, as in one of the cases reported.

When the period of latency between the last conception and the development of chorionepithelioma is short, diagnosis of this condition is generally made but when the period of latency is very long, clinical diagnosis is much more difficult. Several cases have been reported where the patient has come under observation for symptoms due to secondary growths, either in the lungs, brain, bones or elsewhere. In very many cases the chief symptom has been haemoptysis, and diagnosis of pulmonary tuberculosis, dry haemorrhagic bronchiectasis or mitral disease has been made and the true nature of the condition demonstrated on x-ray examination of the chest. Several cases have been reported in which cerebral metastases led to a diagnosis of brain tumour and only on histological examination was attention drawn to the primary site.

Description of the cases

Case No 1 —A married female aged 28 was admitted for almost continuous bleeding for some 8 months. She had two previous normal full term deliveries, the last being 4 years ago. Her last normal menstrual period was about 16 months ago. After a period of 8 months' amenorrhoea, the patient commenced to have reddish vaginal discharge and, according to her, about 8 months before she passed clots and some white solid masses. She was quite definite that a foetus was not passed at that time. Since then she was getting irregular attacks of vaginal bleeding with reddish discharge in between. Fifteen to twenty days before admission, she had a very profuse attack of bleeding for which she had been plugged by a doctor.

On admission there was no vaginal bleeding. Her general condition appeared to be weak and she was anaemic. Nothing abnormal was detected on examination of respiratory, circulatory and central nervous systems. The examination of blood showed 34 millions RBC, 45 pc Hb and WBC 8,100. Nothing abnormal was detected on examination of urine. Her blood pressure was 104/70 mm of mercury. Secondaries were not detected on x-ray examination of the chest.

No tenderness, rigidity or growth was found on abdominal palpation. There was no shifting dullness. On vaginal examination, the cervix was pointing downwards and forwards, pale, smooth, firm and mobile. The uterus was found to be anteфлекed, slightly larger than normal, smooth, soft and not freely mobile. Nothing

abnormal was detected in the fornices. A mass, 1" x $\frac{1}{2}$ ", was palpated in the right anterolateral wall of the lower third of the vagina, which on speculum examination was found to be of reddish blue colour, sessile and of firm consistency. A diagnosis of chorion-epithelioma was made. Friedmann's test was negative. In view of the history and secondary vaginal metastases, abdominal pan-hysterectomy was performed. Free blood was not found in the peritoneal cavity. The uterus was thinned out at the fundus along the anterior wall and the right cornu. Several arterial vessels began to spurt from the thinned out uterine wall. Pan-hysterectomy was performed in the usual way.

For a few days after the operation, the patient had a rise of temperature. On the twenty-first day after the operation the patient had severe vaginal bleeding from the metastatic growth which was not controlled by plugging and underrunning sutures had to be put in. Blood transfusion was given, and the patient was getting on well, when a second similar attack of bleeding occurred 14 days later. The patient was transferred to another Hospital for irradiation of the vaginal growth. She died there a few days later. Post-mortem was not available.

Friedmann's test was again carried out after the operation, and was found to be very strongly positive.

Case No 2—A married female, age about 30, was admitted for continuous bleeding of seven months' duration. She had eight full term deliveries and three abortions. Her last regular menstrual period was about ten months ago. After a period of three months' amenorrhoea, she started bleeding. The bleeding was continuous but of varying intensity. She also complained of attacks of colicky pain in the lower abdomen for one month. The pain had ceased one day before admission, but the bleeding was continuous and more profuse.

On examination her general condition was found to be unsatisfactory and her nails, conjunctiva and tongue were pale. Examination of blood showed 38 millions R.B.C., 48 p.c. Hb., C.I., 0.63, and 7,800 W.B.C. Nothing abnormal was detected in the urine. Her blood pressure was 120/70.

No tenderness, rigidity or growth was found on abdominal palpation. On vaginal examination, the cervix was pointing downwards and backwards, and was soft. A spongy mass was felt in the cervical canal. Uterus was anteverted, about the size of an eight weeks' pregnant uterus, and soft in consistency. Nothing abnormal was detected in the fornices.

On speculum examination a spongy mass was seen in the cervical canal. The mass was not fragile.

Diagnosis of placental polypus was made. Friedmann's test was performed after a histopathological report on the excised polypus showed an early chorionepithelioma. The report was positive with 20 c.c. of urine. Abdominal total hysterectomy was done, but both

the appendages were left behind. There were no post-operative complications.

The patient was sent to another Hospital for deep x-rays. She was seen a few months after the operation and was found to be well. X-ray examination of the chest could not be done at this time. She has not reported since then.

Case No. 3 — A married female, age about 35, was admitted for irregular bleeding for two months. She had six previous full term normal deliveries. On retaking her history after operation and pathological diagnosis, it was revealed that she had an abortion about nine months previously and irregularity of menstruation had set in since then but was more marked for the previous two months.

Her general condition was satisfactory. There was nothing abnormal detected on abdominal palpation. On vaginal examination the cervix was directed downwards and backwards, and was hard and mobile. The uterus was anteverted, slightly larger than normal, smooth, hard and mobile.

Friedmann's test was not performed, either before or after the operation. Pre-operative diagnosis of 'chronic metritis' was made, and abdominal total hysterectomy was done, but the appendages were left behind. There were no post-operative complications. Deep x-rays were given after obtaining the pathological report. The patient was asked to report every three months but did not come for further observation.

Differential diagnosis Some of the conditions for which it may be mistaken are —

- (1) *Local Pelvic causes* a Metropathia haemorrhagica b Placental polypus c Chronic metritis
- (2) *Pulmonary Conditions* a Pulmonary tuberculosis b Dry haemorrhagic bronchiectasis c Mitral disease
- (3) *Cerebral Conditions* a Encephalitis b Brain tumour

Curettage — Curettage, as a method of diagnosis, has advantages as well as disadvantages. It should always be done in a well equipped operation theatre where every kind of help is available. Excessive bleeding may occur during this simple operation, requiring packing of the uterus. Perforation of the uterus may occur during dilatation or during curettage due to the destruction of the wall by the malignant growth. This would almost certainly have occurred in one of our cases. (Cases have been reported where infection has followed curettage sometimes with fatal results.) Histological examination of the curetted material is helpful in prognosis as well as in

treatment, but in some cases, no evidence of its presence is detected in curetted material. In some cases complete recovery has occurred following curettage, but Ewing is of the opinion that such cases were probably of 'syncytial endometritis' and not cases presenting a histological picture of 'chorio-carcinoma'

Zondek-Aschheim Test—The Zondek-Aschheim test is preferable to Friedmann's test as the former is more suitable for the quantitative estimation of gonadotropic hormone. Generally the Zondek-Aschheim test becomes negative within a month after full term delivery and its persistence after a month in a female who is bleeding irregularly is to be regarded as suspicious. After spontaneous evacuation of a vesicular mole, the Zondek-Aschheim test may remain positive for as long as two months, and its value is limited when irregular bleeding occurs within two months after evacuation of a mole. In such cases curettage is necessary, not only for histological examination but also for ensuring complete evacuation of uterine contents. The Zondek-Aschheim test should become negative within a month after curettage and a strongly positive reaction after a month is of grave prognosis. Of the four cases reported, the Zondek-Aschheim test was done in two, one came with acute symptoms and was operated upon immediately, and diagnosis was made in the other by histological examination after hysterectomy was performed. In one case, Zondek-Aschheim test was reported as negative before the operation, but was found to be strongly positive when it was repeated after the operation. In the other case, Zondek-Aschheim test was not done before the operation but was performed after the histological diagnosis had been made. It was then found to be positive with 20 c.c. of urine.

Extensive Metastases without trace of Primary Tumour in the Uterus—Since Zagorjanski Kessel described 9 cases in 1902 in which there was no primary tumour in the uterus, many more have been reported. De Zalka reviewed many more in 1928, and added one of his own in which there were secondaries in the left ovary, liver, lungs and elsewhere without a primary tumour in the uterus. Novak, in an article contributed in 1930, gave a comprehensive review of this type.

Meyer in 1928 reported two cases in which curettage had been performed soon after the expulsion of a vesicular mole,

Hysterectomy, performed in one of them, following excision of a chorio-epitheliomatous growth from the anterior lip of the cervix, failed to show any trace of hydatidiform mole or chorion-epithelioma. In the other case, death occurred from streptococcal infection within a month after curettage had been performed. At post-mortem, no trace of chorionepithelioma was detected in the uterus.

Novak offers three possible explanations for cases in which primary uterine growth is absent. Firstly, that the distant growths are of teratomatous origin, particularly in those cases in which definite history of pregnancy is not obtained. Ewing states, 'with few exceptions the cases of primary ectopic chorioma in the female have been clearly derived from an ectopic pregnancy and a definite gestation sac or a uterine pregnancy was demonstrated but, in a few cases, this connection has not been conclusively shown. In the absence of other unmistakable evidences of pregnancy, chorioma may have to be referred to a teratomatous origin'. Secondly, such metastatic growths may arise from malignant degeneration of trophoblastic emboli, which are known to occur in normal conception, even when the placenta itself shows no malignancy. Thirdly, curettage may have been responsible for the disappearance of the primary growth from the uterus, although death may have occurred due to distant metastasis.

Ovarian and Pituitary Changes Associated with Chorion-epithelioma and Hydatidiform Mole. Statistical data regarding frequency of multiple lutein cysts is not accurate in so far as such statistics are largely based on abdominal and vaginal palpations, while ovarian changes are very frequently demonstrated on histological examination when there have been no palpable cysts. Novak quotes the figures of Coltalorda that lutein cysts were present in 59 p.c. of the cases of hydatidiform mole and in 94 p.c. of the cases of chorionepithelioma.

Macroscopically such cysts may assume enormous size and in some cases troublesome pressure symptoms have occurred. They may be as large as a man's head or they may be small, the characteristic changes being demonstrable only on histological examination. They may be unilocular or multilocular and the contained fluid is most often clear. Generally, spontaneous retrogression of these ovarian cysts occurs, but Joseph and

Rabeau have reported a case in which no ovarian cysts were present at the first operation, but at the second operation six weeks later the right ovary was about the size of a hen's eggs. Harold reports a case in which small cysts increased in size six weeks after the expulsion of the mole.

Microscopically there is marked hypertrophy of the theca interna cells which have undergone lutein transformation. Novak has reported a case in which there was luteinisation of both granulosa as well as theca interna cells. The degree of luteinisation as well as the character of luteinised cells differs, but in the majority of cases such lutein transformation is due to theca interna cells.

The cause of these ovarian changes is not yet definitely established. At the present time, the majority of workers believe that the ovarian changes are due to the exaggerated trophoblastic stimulus and very few still hold the previous view that ovarian changes cause exaggerated trophoblastic proliferation resulting in hydatidiform degeneration of the ovum. As a result of the study of Zondek, Aschheim and others it appears that increased trophoblastic response causes exaggerated activity of the gonadotropic hormone of the anterior pituitary gland and this excessive secretion of the sex hormone of the anterior pituitary, produces an excessive lutein response in the ovary.

General Prognosis of Chorionoma—It appears that prognosis depends not only on the histological character of the growth but also on the type of preceding pregnancy. The table given from the analysis of 188 cases by Teacher demonstrates very clearly the relation of prognosis to the preceding conception.

Preceding condition	Total	Deaths	Recoveries	p c of recoveries
Hydatid mole	73	30		
Abortion	59	78	34	46.6
Labour at term	40	30	20	57.9
Tubal or ovarian	7	5	10	10.4
Total	188	121	65	34.2

On histological evidence it appears that the lowest mortality is recorded in cases of so-called 'malignant' moles (chorioadenoma of Ewing) and syncytioma, while the mortality is very high in typical chorio-carcinoma cases. In 1907, Schmauch found that of 108 fatal cases 79 i.e., 73 p.c., could be classed

as chorio-carcinoma Ewing from a study of the cases holds the opinion that a fatal result in typical chorio-carcinoma is directly due to malignancy, while in the other histological types death is due to haemorrhage, infection and cachexia, and not due to the progressive growth of the tumour

Treatment —No sooner diagnosis is made, pan-hysterectomy should be undertaken. If the patient is anaemic due to previous vaginal bleeding a blood transfusion may be required before the operation. Whether the vaginal or the abdominal route is to be preferred, is a debatable point. When the uterus is very much enlarged or there are large bilateral ovarian cysts then the abdominal route is the only possible method. Even in those cases where the uterus is small in size the abdominal route is to be preferred, because by this route clamping of the infundibulopelvic ligaments with the ovarian blood vessels within them is possible as the first step of the operation. This is necessary, when it is remembered that invasion of blood vessels in the uterine wall by the invading chorionic tissue is the rule and the handling of the uterus prior to clamping of the blood supply of the uterus may cause dissemination into the systemic circulation. There is yet another reason for choosing the abdominal route and that was noted in the third case reported. On opening the abdomen, and even before commencing the operation, blood vessels from the thinned out uterine wall started spurting, and clamping off of the blood supply was carried out without much loss of blood. This would not have been easy if the vaginal operation had been undertaken. It is not necessary to remove the cellular tissue of the broad ligaments with the lymphatic glands as there is very little lymphatic permeation.

Pan-hysterectomy is not contra-indicated with local vaginal or vulval metastatic growths. When metastases have occurred in distant organs, such as lungs, liver or brain, pan-hysterectomy is of doubtful value. It is the opinion of some writers that even in the presence of such distant metastases pan-hysterectomy should be performed, as it may result in regression of such distant growths. Ewing sums up the prognosis in the following statement 'It is therefore evident that neither pulmonary nor vaginal metastases carry a necessarily fatal prognosis, although it should be emphasized that a great majority

of the patients with cough and haemoptysis die. The gravity of vaginal metastases is considerably the less serious, and the occurrence of quite harmless vaginal emboli of cells and villi should be kept in mind.

Local metastases in the vagina and vulva may be left without treatment as regression of such growths after pan-hysterectomy is known to occur. In one case in which there was local vaginal metastatic growth, severe bleeding occurred twice at intervals of 14 days after pan-hysterectomy had been performed. Due to the possibility of such unexpected bleeding, and as excision is comparatively a simple procedure it is prudent to excise or radiumize such local growths and not to leave them untreated.

Radium therapy has produced a small number of cures, but in view of the differences in histological classification such reported cases require further investigation regarding the histological variety. It is reasonable to suppose that 'syncytioma' may react favourably to curettage followed by intrauterine radium, but the typical chorionepithelioma is a highly malignant growth and response to radium is unlikely to be as favourable as in the relatively benign varieties. Besides, there is a definite risk of severe secondary haemorrhage occurring in such vascular growths after intrauterine irradiation.

Causes of Death (1) Progressive malignant disease, (2) anaemia due to repeated haemorrhages from the vagina or from the lungs, due to secondary metastases, (3) shock following radical operation, (4) haemoperitoneum, (5) infection following curettage and (6) cerebral symptoms due to central metastasis.

Case No 4 A married female, age between 35, was admitted for swelling of abdomen following upon a period of three and a half months' amenorrhoea. She had previously six full term normal deliveries, the last child being born three years ago. After a period of three and a half months' amenorrhoea, she noticed a swelling in the abdomen which rapidly increased within a month and began to cause her respiratory distress.

On admission there was no vaginal bleeding. Her general condition appeared to be weak. On abdominal palpation, a tense swelling was found rising out of the pelvis and extending to about three fingers above the umbilicus. There was no external ballottement. The swelling was tender on palpation. On vaginal examination the external os admitted one finger. The abdominal swelling was found

to be due to uterine enlargement. There was nothing abnormal detected in the fornices.

An immediate operation was decided upon, due to the respiratory distress which was causing great discomfort to the patient. The pre-operative diagnosis was vesicular mole. On opening the abdomen, free blood was not found in the peritoneal cavity. A subtotal hysterectomy was performed in the usual way. There were no post-operative complications.

Pathological report was malignant vesicular mole. Although the ovaries were not enlarged, lutein cysts were detected on microscopic examination of the ovaries.

Professor R. G. Dhayagude gave an account of the specimens of chorionepithelioma received in the Pathology department since the year 1929. He described the naked eye characters of the growth in which the uterus was not very much enlarged. The growths belonging to either of the following four types were commonly present: (1) A haemorrhagic growth slightly raised above the surface, (2) a mass like a haematoma filling the entire uterine cavity, (3) a polypoid appearance, and (4) a growth showing villous sort of appearance near the surface but infiltrating into the uterine musculature. Very rarely the entire growth was situated deeper in the muscle. Diagnosis of these was made by a curettage and a biological test. Diagnosis by curettage may be very easy or in some cases very difficult. Proliferative changes in the trophoblast were present in the hydatidiform mole, malignant mole and in a chorionic epithelioma. The criteria of malignancy must be fixed, in literature one finds that a number of cases which probably were not chorionepithelioma have been diagnosed as such. Figures as regards the mortality rate after operation in such cases cannot be relied on. (1) Lack of differentiation into a villus, (2) freshness of the cells, (3) anaplastic changes in the Langhan's cells, (4) infiltration of the tissue, (5) destruction of the muscle, are some of the points which have to be taken into consideration in arriving at the diagnosis. Mere presence of chorionic cells in the veins and in the sinuses was not indicative of malignancy. One cannot depend on one finding alone, the whole picture must be taken into consideration.

As a biological test the original A-Z test was better than Friedmann's test but due to practical difficulties the latter was performed in this institution. He then quoted some of the mis-

leading results due to wrong samples, unsuitability of the animal etc. In cases of placental polyp the test was found to be weakly positive in two cases with 20 c.c. of urine. In a case of chorionic epithelioma the test is found positive in 0.01 c.c. of urine or even less. The interpretation of the findings must be carefully made as in the course of normal pregnancy at some stages the amount of prolan excreted in the urine might be more than 200 000 mouse units quantities which were said to be diagnostic of hydatidiform mole.

Besides, undoubted cases of chorionepithelioma have been described by Schumaker and others in which the A-Z test on repeated occasions was negative. These cases are difficult to explain. However, it must be mentioned that they were rare and that A-Z test is one of the most valuable adjuncts in the diagnosis of this dreadfully malignant disease.

Dr Dhayagude then explained a few points on each of the numerous specimens he had brought to illustrate the condition.

Discussion

Dr J Jhirad cited two cases. The first was in 1934 with irregular bleeding following a vesicular mole. Diagnostic curettage was done; there was sharp bleeding during the operation. On digital exploration a doughy area was felt at a cornu. The curettings were scanty. Pathological report on curetted material indicated chorion-epithelioma. Friedmann's test was strongly positive before and after curettage. The pan-hysterectomy specimen showed a small intramural nodule. The second case also had irregular bleeding following a vesicular mole. Curettage was done and the pathological finding was chorionepithelioma. Blood transfusion and pan-hysterectomy was done with satisfactory results.

Regarding the value of diagnostic curettage and the biological test she felt that both methods used in conjunction would be helpful. Referring to the treatment she wondered how far one was justified in sacrificing the ovaries in a young woman in view of the fact that chorionepithelioma unlike other malignant conditions varied so much in its malignancy.

Dr N A Purandare reviewed the development of the ovum and its covering membranes. He further described a personal case which was admitted as chorionepithelioma, for pan-hysterectomy. But as the curetted material was not soft and friable but firm and hard, the diagnosis was changed to placental polypus. Histopathological examination however revealed a chorionepithelioma.

After the scraping, the patient felt better, stopped bleeding and decided to leave the hospital. However, bleeding started again just before the day fixed for her departure and hysterectomy was done.

The patient made an uneventful recovery but on the 20th day she developed fever, cough and haemoptysis. Her condition rapidly worsened and she died. On autopsy, metastasis were found in the lungs, liver, spleen and kidneys. Dr Purandare further described a case where a patient passed a vesicular mole and suddenly developed acute pain in the abdomen, some months later, with all signs of internal haemorrhage. On lapiotomy, a bleeding spot was observed on the posterior wall of the uterus at its lower part. The bleeding was completely controlled by a stitch. The patient subsequently became pregnant and delivered naturally.

Rational Therapeutics

THE MEDICAL TREATMENT OF BLEEDING FOLLOWING AMENORRHOEA

By

B N PURANDARE

M D, F R C S E

BOMBAY

This type of uterine bleeding is quite a frequent occurrence in every day practice and the nature of the diseases manifesting this symptom is so varied that one must have a definite diagnosis before the treatment can be started on the sound bases and along the correct lines. The type of lesion, one is likely to encounter with this symptom, will naturally vary with the age of the patient. In the early teens, the condition is a manifestation of dysfunction of the ovaries that has received a most fascinating name of metropathia haemorrhagica or anovular menstruation. During the first few years after the menarche a girl may get uterine bleeding but it need not be associated with ovulation. Some are fortunate in having the periods of bleeding at exactly monthly intervals and not associated with much blood loss each time. But other unfortunate individuals may either get these anovular menstrual floodings too frequently with short intervals of two to three weeks, or there may be periods of amenorrhoeas of 45 to 60 days followed by little yet prolonged bleedings for a fortnight or so. This latter condition is the result of hyperoestrinism without the production of the corpus luteal hormone. The individual goes on collecting oestrin in the body till it reaches sufficiently high to inhibit the anterior pituitary gland. Thus the further stimulation of the ovaries for the production of oestrin is indirectly removed. This is followed by a drop in the oestrin level in the blood and the patient gets the bleeding from the uterine endometrium which is then existing in the stage of marked proliferation. These rhythmic ups and downs in the oestrin level in the blood may, as a matter of fact, be noted every fortnight or so and, as

stated above, one of the drops is usually followed by uterine bleeding. Outwardly these cases may simulate so closely with very early cases of abortion that one may often find the patients giving the history of a series of abortions in a year while at the same time the P. V. examination shows no evidence of the uterus having been pregnant any time before.

A similar condition may also be noted at the time of menopause but the problem of treatment for the condition at that age is not so difficult as one can then use drastic measures to stop the menstruation permanently as will be discussed later. In the younger individuals, especially unmarried persons, it is however a most difficult condition to deal with and it tries all the skill and the patience of the physician in the medical treatment which one has to try at its full extent at that age.

But it must be always borne in mind that a similar symptom complex may be produced at both the extremes of menstrual epoch by the rare tumours in connection with the ovaries, namely, granulosa cell tumour and theca cell tumour, the latter being seen only after the menopause. Hence there is an absolute need of a thorough internal examination as these tumours require immediate surgical removal.

During the child-bearing period among married women, the problem of threatened, incomplete and complete abortions has also to be decided before the treatment is started. But a clue can be obtained from the fact that in such patients the history is of a short duration in the sense that there is only one period of amenorrhoea followed by bleeding without a previous history of recurrence of such phenomena, unless of course, one is dealing with a case of habitual abortions. But even in the latter, the patient is menstruating quite regularly in between the abortions.

One more condition that must be kept in mind is the corpus luteum persistence which is associated with periods of amenorrhoea followed by a prolonged bleeding. The uterus bleeds from a secretory endometrium and the bleeding is a true menstruation according to the real meaning of the term. It is in fact a condition like pseudo-pregnancy and requires quite a different treatment altogether. The Gynaecological surgical emergency arising from extra-uterine gestation rupture must also be considered along with all the above mentioned conditions as

it will be profitless to treat it medically and unnecessarily a life may be lost in doing so

One can make a correct guess of the existing condition by analysing the associated symptoms in details. In metropathia, the uterine bleeding is comparatively less at a time but it is unusually protracted and is not accompanied by pain unless the condition has existed for a long time and the endometrium develops polyp. With ectopic gestation the external bleeding is comparatively very little and in some cases lasting over a long period, but severe pain in the lower abdomen is characteristic and is associated with marked anaemia out of proportion to the external bleeding. In a case of uterine abortion, however, both the pain as well as bleeding may be excessive and, unlike ectopic gestation, may be detected in a patient who is having repeated pregnancies.

Now as regards the treatment, it must be stated at the outset that the conditions like ectopic gestation, granulosa cell tumour and theca cell tumour require a surgical removal and the medical treatment is needed for the co-existing anaemia only. The persistence of a corpus luteal cyst may require a diagnostic curettage to distinguish it from metropathia haemorrhagica or from a case of an abortion since by that way alone can one come to the correct diagnosis by finding on histological examination a well developed secretory phase without the presence of chorionic villi. The patient should at first be treated as a case of menorrhagia with ergot and calcium etc., and if in spite of medical treatment the uterine bleeding is not under check a thorough curettage may have to be resorted to from curative point of view. The thickened endometrium in an exaggerated secretory phase takes a long time for its desquamation and the whole process may be hurried up by the removal of that material by means of an uterine curette.

The patient with a threatened abortion requires an absolute rest in bed and a dose of general and uterine sedatives. A better way will be to give the patient an injection of $\frac{1}{4}$ gr morphia which helps to quiet down mentally the excited patient. The effect may be further continued by repeated doses of bromide, chloral hydrate and tr opi as often as required. But for no reason must the patient leave the bed and should avoid straining at the stools. Mild laxative is often helpful and the bowels

can further be opened by daily enemata. The sensitivity of the uterine musculature can be reduced by small doses of corpus luteal hormone given in the form of injections, each two to five mgm daily till the bleeding stops. Yet one should use the preparation with extreme caution and should use smaller doses as the use of big ones may be followed by painless abortion and profuse post-abortion bleeding.

Those who suffer from repeated abortions especially within the first three months of pregnancy require hormonal treatment provided the general conditions like chronic nephritis, hypertension, chronic pulmonary disease and cardiac failure, and local lesions like chronic retroversion and under developed and infantile uterus are ruled out by thorough examination and investigations of the patients. For these patients, the hormonal treatment with progesterone should be started soon after the missing of a period and should be continued upto the end of the fourth month till actually the placenta has started the secretion of various hormones in sufficiently large quantities. It is also found advisable to treat this type of patients of habitual abortions both from the prophylactic and curative point of view with the prolonged administration of vitamin E preparation as soon as the conception occurs. During the actual bleeding phase big doses of vitamin E as two capsules t.d.s. must be given till the bleeding is well under control. Later on a maintenance dose of one capsule per day may be continued till the end of sixth to seventh month of pregnancy.

A few patients of habitual abortions are found to pass the products of conception without any appreciable pain. In these individuals, the uterus is lacking in its usual tone and thus favours the easy separation of the ovum and the formation of a blood-mole. These persons are benefited by small doses of uterine tonics, e.g., *Eligodex* minm 3, *Tinct Nux Vomica* minm 3, and *Calci Lactas* gr. 10 per each dose of the mixture given thrice a day. The use of uterine sedatives such as Progesterone is not beneficial in such individuals, in fact it may favour the separation of the ovum.

The cases of incomplete abortion with bleeding require more immediate surgical treatment. In the presence of an associated infection it is by far advisable to treat such cases on usual medicinal lines. A thorough course of sulphanilamide

preparations, both orally and by injections, should be administered along with ergot or pituitary. Hot vaginal douches and short wave exposures to the pelvis will often help to resolve the inflammation. But in no case should any surgical treatment be employed so long as the patient is showing manifestations of local sepsis. In the presence of a mild local infection, the Hobb's method of intra-uterine glycerine irrigation, as employed in cases of menorrhagia, is worth the trial. It also promotes the expulsion of any septic bits of the products of conception left behind.

Complete abortion, as detected by the closure of the cervix and the small size of the uterine body, may further require purely medicinal line of treatment. The patient should be in bed at least a week following the abortion and should take uterine tonics to favour the involution of the uterus. These may be very conveniently given in the form of tablets Neogynergen b d. If possible hot vaginal douches may be taken by the patient to hasten further the involution process.

Metropathia haemorrhagica is the most intractable condition to deal with especially when a cure is to be effected by adjusting the menstrual rhythm back to the usual monthly interval. It is a disease which very often gets itself corrected spontaneously and the medicine, that is used at that time, often gets the unmerited credit. As it is the result of disturbed metabolism of ovarian sterols the local operative treatment very rarely succeeds in correcting the ovarian cycle. No doubt the removal of the endometrium, which is unhealthy and thickened, may temporarily cure the condition since it is supposed that for the complete metabolism of oestrogens the presence of healthy endometrium is most essential. Within a few months after curettage, however, the endometrial hyperplasia and its patchy necrosis are likely to recur with the reappearance of irregular menstrual rhythm. In an elderly person, in whom one can safely put a stop to the function of menstruation, the treatment is not so difficult as both the operative means and the radium treatment are helpful in getting over the condition. The real difficulty is with the young girls at the time of puberty or with women during the early part of the child-bearing age when the destruction of the ovarian function even as a temporary measure is rather a risky problem. These patients really deserve

the medicinal and hormonal treatment and one is fully justified in giving trial to them before the operative interference is thought of since the cancer of the body of the uterus at that age is unknown

It must be evident that elderly persons above the age of forty or forty-two can be treated with radium application for putting a stop to the ovarian function altogether. As in the case of menorrhagia at the menopause, the radium is preferable to x-ray treatment as one can examine the uterine endometrium microscopically and be sure that he is not dealing with an early case of malignancy of the body. From the recent investigations by various workers it is becoming more and more evident that the endometrial hyperplasia at or after the menopausal age has a definite relation to malignancy of the body. This fact makes it absolutely necessary to have the histological examination of every bleeding endometrium to rule out carcinoma of the body before any sort of treatment is started. The use of hormones to treat the condition without these investigations at that age is both unsuitable and risky as unnecessary time may be lost in treating these cases purely palliatively without being fully investigated. Moreover, in the early stages of the cancer of the body there is not much appreciable enlargement of the uterus and the irregular bleeding with period of amenorrhoea may be mistakenly diagnosed and treated as a case of metropathia. Patients between the ages of thirty and forty deserve both the hormonal and operative treatment but not radium or deep x-rays. The operation of dilatation and curettage can be done repeatedly as stated above and if the patient is ready to have the complete stoppage of menses, vaginal removal of the uterus by sub-total or total hysterectomy, especially in multiparas, is likely to cause the least inconvenience to the patient with practically negligible mortality. In so far as ovaries are conserved the ovarian function is preserved, there being no chances of inducing premature menopausal symptoms and turning the individual into a nervous wreck.

The younger patients from the age of menarche upto the age of forty are the fit cases for the medicinal and hormonal treatments. Since the condition is produced by the failure of ovulation and excessive production of oestrin in the body the problem can be attacked in various angles. Means may be used

to favour ovulation and lutenisation with the help of Gonadotropic hormones or to secure the progestational phase in the pre-existing hyperplastic endometrium by progesterone supplementation therapy, to bring about the atrophy of the thickened endometrium by the use of male hormone, to correct the metabolism of oestrin by giving big doses of corpus luteal hormone and to reduce the permeability of the capillary walls and to increase the coagulative property of blood by the use of vitamins K and C, calcium, congo red, coagulin-Ciba, arrhemapectins and moccasin venom injections. The local oedema in the endometrium can be relieved to a great extent by the use of intra-uterine glycerine irrigations and it is often found to succeed in many cases. Some workers like Hambleton and others, consider the uterine bleeding as a result of fall in the oestrin level in the blood and advocate the use of oestrin during the bleeding phase but considering the relation of the endometrial hyperplasia to malignancy of the uterine endometrium such a procedure appears risky especially in elderly persons. The use of oestrin is put forward with an argument that the oestrin present in the patient's body is abnormal and is the end result of disturbed metabolism and by giving active and normal oestrin the function of the endometrium can be brought back to normal, and hence the simultaneous administration of normal oestrin and progesterone helps to improve the condition and regulates the ovarian sterole metabolism.

As stated previously, small repeated transfusions during the bleeding phase are also beneficial especially if taken from a pregnant patient in the second or third month of pregnancy or from a male person. The injection of posterior pituitary extract is often found useful as an empirical method. The thyroid extract may be used to depress the ovaries in the excessive oestrin production during the period of amenorrhoea.

Thus during the phase of amenorrhoea, patient can be given anterior pituitary gonadotropic hormone in the form of a course of Prephysin or serogan injections. Five injections of 200 units each should be followed by another prolonged course of chronic lutenising hormone Antuitrin S or Physostab till the bleeding begins. At the same time patient should have vitamin C calcium and thyroid extract by mouth. During the bleeding phase the

simultaneous injections of Antuitrin S and Progesterone must be given till the bleeding is under control. By this latter treatment though it is not possible to produce a picture of secretory endometrium in every case yet there is often seen a therapeutic good result. If required the patient can also be treated by male hormone injections, 25 mgm each till the bleeding is under control.

The use of Adrenal Cortical Hormone is also advocated during the bleeding phase on the principle that its action is similar to progesterone and male hormone. But its present cost makes it impossible to give a prolonged trial.

Every bleeding case requires a thorough examination of blood including the blood coagulation time, blood sedimentation rate and fragility of R B C. and the capillaries. When other treatments fail the exposure of the splenic area to deep x-rays may prove useful in some of the intractable cases.

If in spite of medical treatment no improvement is noted recourse may be had to dilatation and intra-uterine radium application. In an elderly patient an exposure of 1,200 mgm hours is quite sufficient to produce castration but in younger individuals smaller doses of 200-300 mgm hours may produce temporary sterilisation with its associated risks. Here one would like to emphasize the importance of sub-total Hysterectomy per vaginum especially in a multiparus individual, in whom marital life is to be maintained.

Critical Notes and Abstracts

WEIL'S DISEASE (SPIROCHAETOSIS ICTERO-HAEMORRHAGICA)

W F Ashe, H R Pratt-Thomas and C W Cumpe (Medicine, 1941, p 145-210) give a complete review of the American literature on Weil's Disease and give an abstract of the world literature on the subject and report seven cases of their own

Weil's disease is a specific infection caused by *Leptospira Icterohaemorrhagica* and characterised by a sudden onset with profound prostration, aching muscular pains, a high fever and frequently with subsequent development of jaundice, evidence of renal failure and a haemorrhagic tendency

History Weil described his four cases in detail in 1886, but prior to this, a few epidemics of jaundice were described, which in some respects resemble the disease as we now recognise it

Nomenclature The authors prefer to use the term Weil's disease rather than the alternatives suggested by some, viz, *Leptospirosis Icterohaemorrhagica* and *Spirochaetal Jaundice* because there are other strains of *leptospira* which are pathogenic to man and because in 50% of the cases of Weil's disease jaundice is conspicuous by its absence

Incidence Since Wadsworth first discovered and proved a case of Weil's disease in America in 1922, 67 cases have been reported including 7 cases by the authors. In 1939 a review of 374 cases appeared from the Netherlands. The number of cases reported from England, France and Germany runs well over a thousand. It has been found to be relatively common in Denmark, Australia, Egypt and South Africa and cases have been reported from almost every civilised country in the world. The authors explain the paucity of the American records in spite of the organism, the vector and the susceptible persons being found with the same frequency as in Europe by suggesting that numerous cases are missed because most doctors think that it is a very rare condition and hence do not suspect it. Few physicians are aware that only about 50% of the cases have any jaundice. Again, there are not enough laboratories equipped to establish the diagnosis and even in the laboratories which exist, familiarity has not been obtained with the precautions that must be taken in establishing the diagnosis in each of the distinct stages of the disease.

Mode of Infection *Leptospira icterohaemorrhagica* is found in the excreta of more than 10% of the adult common gray rat but in addition, it has also been found in dogs, field mice, cats, pigs, foxes and horses. The vast majority of the infections occur through direct contact with the excreta of rats. The organism can live for over three weeks in stagnant water which is neutral or slightly alkaline. Water infected with the excreta of spirochete carrying rats may in-

fect man through abrasions in the skin, or the nasal mucosa or the conjunctiva. Infection through the gastro-intestinal tract is probably unusual with normal gastric acidity. It is probable that the organism cannot pass through the unbroken skin.

The disease is not confined entirely to the sewer workers but is found in all those who come in contact with infected water. Thus, cutters and cleaners of fish are affected frequently and miners, tunnel diggers, persons swimming in infected pools, butchers and veterinarians are reported to be infected. In Rotterdam, accidental falling in dirty canals has caused infection and in Japan, the disease is common in rice field workers where the sowers of rice have to work in fields flooded with water and in some tropical countries it is not uncommon in sugarcane cutters. One case has been reported of transmission through copulation and one of intrauterine infection of the foetus. Cases have been reported where the immediate contact came from a dog and not from rats. From time to time, cases have been reported of infection from drinking water but these are not all authentic.

Age and sex Being an occupational disease, it is most common in males between the ages of 20 and 40. The seasonal incidence is maximum in the months of July, August, and September in Europe and America and in September, October and November in Japan.

Clinical Features After an incubation period of from 4 to 19 days (average 10 days), the disease runs a clinical course in three stages which run one into the other without a sharp line of demarcation. The first stage is called the septicaemic stage of the disease and lasts from two to nine days, usually five. During this stage the organism is circulating in the blood, there are no specific antibodies in the blood and the spirochete is not excreted in the urine to any appreciable extent. The first stage is said to last up to the onset of jaundice. In non-jaundice cases it is said to last as long as the spirochetes can be demonstrated in the circulating blood.

The onset of the disease can be marked not infrequently to the exact hour, the patient feeling a severe headache, usually frontal but may be bitemporal or occipital, and this is associated with slight chill and severe prostration. Muscular aching of the back, the calves, and the extraocular muscles is pronounced. Anorexia and nausea are soon observed and are persistent. Pain in the abdominal muscles associated with nausea and vomiting suggests an acute abdomen. Cough and hiccough with blood stained expectoration are frequently observed.

Physical examination shows a high temperature (102° to 106° F) with a full rapid pulse but there is some degree of relative bradycardia. The respirations are rapid, the blood pressure somewhat low, the skin hot and dry, and the patient acutely ill. Herpes is unusual and uncommonly one may find a rash but usually it does not appear until the second stage. All the mucosae are congested the conjunctivae suggesting a pink-eye. The lymph nodes are not enlarged. The lungs may be normal or may show patchy consolidation. Usually there is tachycardia but sometimes there is a pronounced brady-

cardia Petechial and ecchymotic haemorrhages occur and haematomas after vein puncture are common. The abdomen though tender is soft and peristalsis is normal. When the haemorrhagic tendency is severe, peritoneal haemorrhages may occur giving all the clinical signs of an acute abdomen but there is always purpura somewhere else also. Not infrequently there is neck rigidity of muscular origin and the superficial and tendon reflexes are diminished. Kernig's sign may be positive in a few cases and the French observers describe a true opisthotonus. Leucocytosis is present from the onset, between 14,000 to 20,000 cells with marked increase in the polymorphs. Myelocytes are not uncommon. There is slight anaemia but the platelets and prothombin time are normal. There is oliguria with albuminuria. Bile and urobilinogen are present in the urine early in the disease. The sputum if present is bloody and the vomitus contains bile and gives a positive benzidine reaction, but frank blood is not seen unless there is epistaxis or haemoptysis. The stool is normal. The spinal fluid shows an increase in proteins and the cells may range from 50 to 1,000, the polymorphs and the lymphocytes being in equal numbers. A pellicle is often formed and the organism cultured from it. The blood urea rises to 50 to 100 mgm per cent and the amount increases rapidly as the disease progresses and may even go upto 150 mgm per cent. The blood sugar and chlorides are normal. With anuria, evidences of profound acidosis may be present.

In this stage the *L. icterohaemorrhagica* may be found by direct dark field examination of the blood or may be cultured from the blood or from the spinal fluid in suitable media.

As the disease progresses, the symptoms and signs increase in severity. On the 5th or 6th day of the disease the temperature falls abruptly to near normal, and jaundice appears. Though the temperature falls, the general condition of the patient is much worse. With the appearance of the jaundice the second stage of the disease begins.

The second stage This is the "icteric stage" but not all cases are icteric. Neither is the term "toxic stage" any more suitable for the mild cases do not show any marked toxicity. For practical purposes, the non-icteric cases pass directly into the convalescent stage. During this icteric stage of about a week the spirochaetes disappear from the blood and appear in the urine and the specific agglutinins and lysins begin to appear in the blood.

Jaundice may appear on any day from 3rd to the 9th day, usually on the 4th or 5th day. The intensity of the jaundice may vary between just detectable icterus and a profound intense bright orange yellow jaundice and the icteric index may rise to 325.

Early in the second stage the renal failure becomes pronounced and occasionally anuria develops. Petechial and ecchymotic spots on the skin and mucosa become more numerous. Vomiting stops early in the second stage. Pruritus is rare. Temperature may rise again. The pulse is relatively more frequent and the respirations are hurried. The general condition of the patient is very toxic and he may be semi-comatose or delirious. The complaint of headache

so marked in the first week is now gone. A morbilliform or scarlatiniform rash is often described in the cases in Europe but is not common in American cases. Pericardial friction, ectopic beats and tachycardia are observed but there is no change in the size of the heart. The heart sounds are muffled and there may appear systolic murmurs. The arterial pressure is low and peripheral failure may appear but the venous pressure is not raised and there is no congestive cardiac failure. The liver is enlarged and tender but the *spleen is not palpable nor is there any lymphadenopathy*. A low grade ileus is common and peristalsis is diminished. Costovertebral tenderness is rarely seen except when there is subcapsular renal haemorrhage. The muscle tenderness is less pronounced.

The white cell count may remain the same or rise with the icteric index, and go up to even 50,000 per cmm. The anaemia is more marked. Coagulation time and the platelet count are not affected. In this stage bilirubinuria supervenes on albuminuria and cylindruria. Stools are whitish. The spinal fluid remains unchanged or may show a slight yellowish tinge. The blood is now sterile.

Death usually occurs between the 9th and the 16th day in the fatal cases. The death rate is about 30%. Death may occur from renal failure, renal and hepatic failure, peripheral vascular failure, or from haemorrhage, toxæmia, or terminal pneumonia. The meningitis rarely if ever kills.

In non-fatal cases the end of the second week brings about a favourable change ushered in by diuresis and there is a gradual retrogression of all the signs and symptoms but at this time *endocyclitis* or *optic neuritis* may occur. The spirochaetes now begin to appear in the urine. During the period of leptospiruria specific antibodies begin to appear in the blood. They can rarely be detected before the 9th day and are usually not of diagnostic titre until the 14th day. Agglutination in dilutions of over 1:300 is considered diagnostic of Weil's disease. By the end of the third week, when the third stage begins, the titre is frequently over 1:100,000 and once attained this high titre is maintained for years.

The third stage. The convalescence, once established, may be rapid, i.e. of one or more weeks or it may be protracted over ten weeks. At any time during this period a relapse may occur lasting for a few days. It is usually mild and rarely fatal. One or all the features of the disease may be represented in it. Two or three relapses are not rare. The most severe complication which may go undiagnosed is a leptospiral vegetative endocarditis. Subacute leucosis is another rare complication.

Diagnosis

The presumptive diagnosis is made from, the classical clinical picture of a fever of sudden onset, with severe headache and muscular pains, with calf tenderness, albuminuria and evidence of urea retention. The onset of jaundice with a declining temperature after 5, 6 or 7 days of illness practically clinches the diagnosis but the positive proof is the demonstration of the causative organism or the agglutination reaction.

In the first week of the disease there is a leptospiral septicaemia and the spirochete can be shown in the blood by (1) dark field examination, or (2) by inoculating a guinea pig intraperitoneally and reproducing the disease. The technique consists of examining blood under dark field illumination with either the usual dry high power lense or the oil immersion lense of the average microscope. The *L. icterohaemorrhagica* is an actively motile spirochete, from 18 to 15 micra in length and 0.5 micra in width. It is tightly coiled and has a sharp hook at one or both ends giving the organism the appearance of a C or an S (*Spirocheta interogans*). It has a three dimensional motility and when present in blood, it is in large numbers. Also incubation at 27 C, in vest-pocket, will frequently increase the number in a given specimen.

When blood from a suspected case is injected intraperitoneally into a young guinea pig, the animal develops jaundice and dies in from 10 to 14 days. The organism can then be seen in the liver, lung and kidney of the infected animal by dark field examination of an emulsion or by staining the sections with Levaditi or Giemsa stain. Alternatively one may aspirate a little fluid from the peritoneal cavity after the guinea pig shows a definite and sustained rise in temperature. In this way diagnosis can be established before the appearance of jaundice or the death of the animal. The animal used for inoculation must be young weighing 175 grammes or less.

In the second week of the disease the blood becomes sterile but the spirochetes appear in the urine and occasionally the dark field examination of the spinal fluid may show the spirochete. The dark field examination of urine is not satisfactory because there are many spirochetes in normal urine. One must therefore depend on the guinea pig inoculation in order to demonstrate the presence of the leptospira in the urine. In order to succeed in this the following technique should be rigidly followed: 60 to 80 c.c. of freshly voided urine is centrifuged at 3000 r.p.m. for 15 minutes and the sediment mixed with 5 to 10 c.c. of normal saline and injected into the guinea pig intraperitoneally. The precautions to be taken are (1) the guinea pig must be young and must not weigh more than 175 gms. (2) Urine must not have stood for more than an hour before inoculation, (3) the urine must be neutral when passed as the organisms are killed in acid or alkaline urine, (4) the peritoneal fluid should be examined repeatedly from time to time after the animal shows a sustained temperature rise.

In the third and subsequent weeks, the leptospira *icterohaemorrhagica* produces specific agglutinins and lytic bodies in the blood of the host in a high titre. In the average case after three or four weeks the blood serum of a patient will agglutinate a virulent culture of the *L. icterohaemorrhagica* in dilutions of 1:10,000 and will not agglutinate any other strain in a dilution more than 1:250. The lytic reactions occur at even higher dilutions. The reaction should be done after the 14th day, and a positive in a titre of 1:300

or more should be taken as diagnostic. From the 10th to the 14th day a rising titre is also diagnostic. Once positive, the agglutination reaction is given by the blood for years, or perhaps indefinitely, with only a moderate fall in the titre. A negative reaction after 30th day of illness rules out Weil's disease. *Leptospira canicola* also produces jaundice in man so that if agglutination is not obtained with *L. icterohaemorrhagica* it should be tiled with *L. canicola* in a case of suspected spirochetal jaundice.

Treatment

A few cases have been treated successfully with soluble and colloidal bismuth compounds. Arsenicals are too toxic to be used and antimony compounds and sulphanilamide have proved useless. Curative horse serum having an agglutinating titre of 1:100,000 or higher is effective in reducing the mortality when given early in the first week. The dose is 60 c.c. The immune serum does not alter the course of the disease though it sometimes diminishes the severity of the symptoms. Convalescent serum or whole blood is also useful.

Prognosis. This is worse with the increase in age, severity of jaundice and the extent of renal failure. A persistent bradycardia and a high sustained temperature in the second week and after are grave signs.

Differential Diagnosis. Enteric fever is ruled out at the onset by the marked tenderness of the calf muscles, the presence of the cells in the spinal fluid and a negative blood culture. La grippe, influenza is the usual diagnosis in non-icteric cases but the absence of immediate relief with the fall in temperature on the 4th, 5th or 6th day goes against it. Catarrhal jaundice is the most important diagnostic problem. The absence of leucopenia, enlarged spleen, and lymphadenopathy should go against it. The evidence of renal involvement, meningeal irritation and the haemorrhagic tendency point to Weil's disease. Yellow fever adds to the difficulties of diagnosis in areas where it is present but the absence of marked flushing and the relative frequency of the pulse with secondary rise in the temperature go against it. Leucocytosis and anaemia are not found in yellow fever.

Pathogenesis. *The nature of jaundice.* Reviewing the literature on the subject the authors conclude that the jaundice is probably due, in large part, to true hepatitis, contributed to by haemolysis and intra-canalicular biliary obstruction. They consider *the renal damage* to be chiefly toxic in origin due to spirochetes rather than the bile. But the exact pathogenesis of renal and hepatic damage is as yet unknown. *The haemorrhagic tendency* is primarily due to capillary damage.

In conclusion the authors emphasise that the reason why the disease is not frequently and sufficiently diagnosed is the absence of fully equipped laboratories with trained men and material to do thorough diagnostic and investigative studies in this disease. It seems that the same remarks truly apply to our country also.

Obituary

JAL PESTONJI PADSHAH

M D (Lon), F C P S (Bom)

1897-1943

On Saturday the 10th of April 1943, there passed away from our midst, after a months' illness from septicaemia, serenely and courageously bourne, Dr Jal Pestonji Padshah—a brilliant physician, a charming colleague, an able and a sympathetic administrator



Dr Padshah belonged to a highly respected and intellectual family. He was born in Bombay on 27th June 1897. He had his early education at the Jabbhoy Bharda New High School, Bombay. He gave promise of a brilliant career even then. The age limit for the matriculation examination was sixteen years. Young Jal would have had to wait for four years before he could appear for this examination. Rather than let him waste four years, his mother took him with the rest of the family to England where youth receives its due recognition.

His career in England was equally brilliant. He studied Medicine at the University College Hospital, London, and held some residential appointments in the same hospital. After obtaining his M D degree of the London University in 1924, he returned to Bombay, unspoilt by his prolonged stay in England.

He started his practice and obtained an appointment as honorary physician to the Gokuldas Tejpal Hospital in 1924. Here he soon distinguished himself as a brilliant diagnostician, an impressive teacher and a loveable colleague. Quiet and unassuming in his ways and endowed with the rare gift of always appreciating the other man's point of view, he gathered round him quite a good circle of friends, well wishers and admirers.

Surely it was not the lure of money that made him sever his long association with the G T Hospital. In the post of the Dean of the K E M Hospital he saw an opportunity for national service. In September of 1942 he took office as Dean of the G S Medical College and

the K E M Hospital, thus succeeding Dr Jivraj Mehta. It was no easy task for any one to prove himself a worthy successor to Dr Jivraj. Dr Padshah's task was further made difficult by the tense atmosphere that prevailed, at the time of his appointment, in the College and the Hospital, as the result of the arrest of the Congress leaders. However, with infinite patience and tact, the situation was smoothed over. The students soon realised that clothes do not make a man. They soon realised that he was a true nationalist and they learnt to recognise the sterling qualities of his head and heart. Some of the students were positively rude to him. But there was no bitterness in his heart. When the University was out to mete punishment to one of the delinquent students, Dr Padshah pleaded with one of the University representatives not to be vindictive. "Right or wrong", Dr Padshah argued, "the student acted according to his convictions. A University should not punish a student for his convictions."

In other instance he made every effort to re-instate a student who had been rusticated because of his misguided activities. Even from his death-bed he expressed his great gratification to one of his colleagues in communicating the news that the student was re-instated. Such forgiveness and charity can only be expected from one who has a genuine love for his students—a real Padshah of a teacher. The loss of the student would be heavy.

In the short space of six months he justified his choice as a Dean. He showed in a large measure the rare gift of administration. His administration was marked by a sense of fairness and justice, a consideration for his staff, rigid punctuality, a definite office-routine and a quick dispatch of work.

He formulated and elaborated a scheme for post-graduate training at the K E M Hospital. This scheme was the result of his extensive teaching experience, his own original thinking and his training and observations in England. It may well be called his "Unfinished symphony."

Dr Padshah was an active member of the Bombay Medical Union, and one of its past vice-presidents. He was on the Council of the College of Physicians and Surgeons, Bombay. He leaves behind him a widow and a son.

We came to know him for a little while. But we mourn his loss, for surely, to have known him was to have loved him.

R N C

News & Notes

ARTHUR JAMES EWINS, F R S

The honour of the Fellowship of the Royal Society has just been conferred on Dr Arthur James Ewins, Director of Research of the May and Baker Laboratories at Dagenham, England. This honour, which is the highest scientific distinction attainable in Great Britain, has been conferred on him in recognition of his outstanding achievements as leader of the May and Baker research team who were responsible for the discovery of M & B 693, which they followed up shortly afterwards with the very similar compound, Sulphathiazole. Since then a new remarkably interesting series of totally distinct compounds have been elaborated by Dr Ewins and termed the 'Amidines' (in the same way that M & B 693, PROSEPTASINE, Sulphathiazole, Sulphanilamide, etc., are called "sulfonamides"). With the introduction of the first member of this new series (which is already available commercially) M & B 744 or Stilbamidine "a very great advance has been caused in the treatment of kala-azar" (IMG June 1942). Other members of this series (M & B 800 or pentamidine, M & B 736 or Phenamidine, etc.) are at present undergoing extensive clinical trial with a view to making them available commercially in due course.

EPILAN (A F D)

Cohen and Associates after a series of experiments with Sodium diphenyl hydantoinate (0.2-0.6 gram daily), either in replacement of Phenobarbital or combined with Phenobarbital, in a number of severe institutionalized epileptic cases, have shown that there is a striking synergism between phenobarbital and sodium diphenyl hydantoinate, the combination being far more effective than either drug alone. The reduction of seizures amounts to at least 50% above the most favourable results obtained without the synergistic use of these drugs.

The Authors strongly recommend the joint use of those drugs (viz a combination like Epilan) in every new case of Epilepsy.

From "The Synergism of Phenobarbital Dilantin Sodium and other Drugs" By B. Cohen, Journal of American Medical Association, 114 480, 1940.

CIBAZOL (CIBA)

The Society of Chemical Industry in Basle (Ciba), in whose laboratories sulphathiazole was synthesized some considerable time back, have now made this important product available to the Indian

medical profession under the name Cibazol. Much interest has been created by this new and relatively non-toxic sulphonamide and its position in sulphonamide therapy has been aptly defined by Prof Fleming at a meeting of the Royal Society of Medicine who states that "It was often assumed that the drug of choice for the streptococcal infection was sulphanilamide, for the pneumococcal sulphapyridine, and for the staphylococcal sulphathiazole. It would be truer to say that sulphanilamide was strong enough to deal with the streptococcal infection, sulphapyridine was rather stronger and able to deal also with the pneumococcal but not with the staphylococcal, while sulphathiazole was still stronger and able to deal with all three." (BMJ, 22nd Feb 1941, p 288)

CORRIGENDUM

In the Case Report by J K Mehta, entitled Bronchogenic Carcinoma, which appeared in our February 1943 issue, the skiagram figure on page 63 was printed upside down. Dr Mehta informs us that the patient reported on died recently and at the post mortem only a fibrotic constriction of the bronchus and marked bronchiectasis were observed.

The Indian Physician

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WHOLE NO 17

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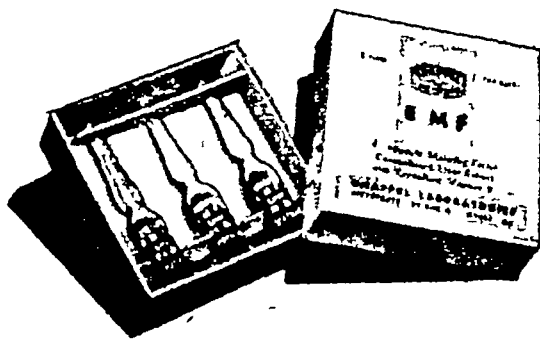
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The Indian Physician

VOL II NO 5

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Let us remember

ON THE EVOLUTION OF RATIONAL THERAPEUTICS

By

N D PATEL

M.D. (LOND), M.B.C.P. (LOND), F.C.P.S. (BOM)

BOVBAL

"There is nothing men will not do, there is nothing they have not done, to recover their health and save their lives. They have submitted to be half-drowned in water and half choked with gases, to be buried up to their chins in earth, to be seared with hot irons like galley-slaves, to be crumpled with knives like cod-fish, to have needles thrust into their flesh and bonfires kindled on their skin, to swallow all sorts of abominations, and to pay for all this, as if to be singed and scalded were a costly privilege, as if blisters were a blessing and leeches a luxury. What more can be asked to prove their honesty and sincerity?"—OLIVER WENDELL HOLMES, Medical Essays, 1888

The ultimate and fundamental aim of medicine is the treatment of disease and as O W Holmes says the suffering humanity is only too willing to carry out honestly and sincerely any treatment prescribed to them, a survey of the origin and growth of therapeutic methods and principles will not only be useful to some of us, whose life-work is to attend the sick, but will also, I hope, sober us in our enthusiasms and prejudices.

The primitive man regarded disease as the work of three agents, first some malicious, mischievous deity, second, some human enemy possessing superhuman powers and practising black magic, third, the offended spirits of the dead, whether of men, animals, or plants. His treatment of disease naturally followed his ideas of causation of disease, the evil deity he tried to propitiate by sacrifices and burnt offerings, the supernatural powers of his human enemy, he aimed to ward off by

appropriate spells and sorcery, similar to those employed by the enemy himself, and the offended spirits of the dead he tried to please by various religious practices, offerings and charms

Savages all over the world cheerfully accept even to-day these three as principal causes of diseases and even in half-civilized and decadent civilized communities, a lingering belief in the supernatural, in the sorcery and in the displeasure of the dead still persists, as shown by the existence of numerous prosperous mediums, spirit societies and healing sects

The first healer of mankind was the medicine-man,—Bilbo or witch-doctor of the savages. He usually combined the offices of the tribal priest, magician and physician in himself. His therapeutic methods consisted of various fantastic manoeuvres, employed to awaken a responsive state of suggestion in the mind of his patients,—in fact, his methods were precisely those employed by the present-day faith-healers, Christian Scientists, osteopaths and a score of other cure-mongers

As man emerged from the savage state and began to think for himself, and build up some sort of civilization, various systems of the medicine also came into existence. The Mesopotamians, the Egyptians, the Hindus, the Iranians, the Chinese,—all these people elaborated very complicated systems of medical principles as their civilizations evolved, but as these principles were not based on exact observation but on some theory of evil, these systems did not prove to be capable of indefinite and independent growth. They lacked elements of continuity and evolution and soon became stereotyped and stagnant

The Greeks, on the other hand, had practised a system of medicine founded on observation which accumulated as time went on. There is a continuity of development in Greek medicine which can be traced from the pre-Hippocratic times to the present-day

The Babylonians treated their patients by putting them in the public places and highways where they were given advice by passers-by, who might have known something about the disease, either from personal experience or from hearsay. The Egyptians were really the first creators of pharmacy. They prepared various preparations of drugs using them side by side with incantations, magic and religious rites, thus combining a primitive drug therapy with suggestion and faith-healing

The Greek medicine also began with priests and temples. About the twelfth century B C, temples were erected all over Greece for the purpose of healing through divine agents. In these temples visions, dreams, water, knife and drugs were used freely, which coupled with faith and suggestion often gave good and spectacular results. "*The Cult of Asklepios*"—by Alice Walton (1894, Boston), and "*The Temple and Ritual of Asklepios*"—by Richard Caton (1900, London), give interesting pictures of medical practice in these temples. Perhaps the most renowned of these was the temple at Epidauros—the ruins of which are still to be seen in Greece, where it stood in a fertile plain surrounded by wooded hills. Sufferers arrived here in crowds from the most distant parts of Greece after long and arduous travel. On arrival, they laid offerings to the god, plunged into the cleansing waters of the fountain and proceeded to various temple rites, the most important of which was one known as the rite of incubation or temple-sleep. The supplicants retired to sleep in an atmosphere of incense and expectation. While asleep, they saw visions, *often the god himself in person*, and they woke up cured in the morning and went home.

That side by side with faith, suggestion, hydrotherapy, and some crude surgery were used as therapeutic agents is clear from the following examples of miraculous cures of Asklepios, taken from Walshe —

Amrosia of Athens, blind of one eye, came as a suppliant to the god. As she went round the temple she laughed at some of the cures, thinking it incredible and impossible that the lame and blind should be cured merely by seeing a vision. In her sleep she saw a vision. The god appeared to her and said that he would cure her, but that in payment she must dedicate a silver pig to the temple as a memorial to her senselessness. After saying this he cut the ball of the injured eye and poured in some drug. When the day came she woke and left the temple cured.

A Man with an Abdominal Abscess. He saw a vision and thought that the god ordered the slaves who accompanied him to lift him up and hold him, so that his belly could be cut open. The man tried to get away but the slaves held him. So Asklepios cut him open, rid him of the abscess and stitched him up.

again, releasing him from his bonds Straightaway he departed cured and the floor was covered with blood

A Dumb Boy came to recover his voice On performing the preliminary sacrifices and temple rites, the temple priest who bore the sacrificial fire turned to the boy's father and said "Do you promise to pay within a year, the fees for the cure, if you obtain that for which you come?" Suddenly the boy said "Yes, I do" His father was greatly astonished at this and told the boy to speak again The boy repeated the words and went home cured

At first the priests who practised in these temples were pledged to secrecy but by the sixth century B C, secrecy was relaxed and Pythagoras wrote a book on the use of squills and the properties of plants, various other books followed on dietetics, hygiene and gymnastics In the fifth century B C Hippocrates (460-377 B C) brought together all the books pertaining to medicine, and adding his own clinical observations, founded the Greek School of Medicine, which is still one of the most precious of our medical heritages But great as Hippocrates was in accurate observation and theorising on humoral pathology, he did little to enrich the therapeutic principles of his time He showed some inclination towards Empiricism when he wrote "In medicine we do not think that it is proper to have recourse to hypotheses, teaching should be accepted from the most simple men if they appear to know something decisive in respect of a given thing It is thus, I believe, that our art has developed Great attention should be given to what happens by chance, if the phenomenon can be confirmed upon several occasions"

But it was in the third century B C that Philinus of Cos and Serapion of Alexandria formulated the laws of Empiricism They recognised three sources of study, namely, chance which furnishes facts, experiments which make it known if it is possible to reproduce these facts and lastly, analogy, by which recognised procedures found useful in the two former cases may be applied to similar cases It may be said that Empiricism held full sway,—in spite of various opposing systems,—such as Methodism, Pneumatism or Animism,—in medical practice till the last century when rational therapeutics based on new physiology and pathogenesis came on the scene

The pharmacy and materia medica were considerably enriched during the Greco-Roman period of medicine (156 B C—

576 A D) The Greco-Roman physicians freely used aconite, poppy, henbane, hemlock, hellebore, arsenic, antimony, iron, the sulphate and acetate of copper, the carbonates of potassium and sodium, nitrate of potassium, alum, calcium, gold, and silver, cantharides, salamanders, vipers and sulphurous, aluminous and saline mineral waters This was the era of polypharmacy and Andromachus of Crete, physician to Nero, compounded a remedy, composed of seventy-two ingredients—in fact all the *materia medica* of his time and called it *theriaca*, which is reputed to have been used throughout the ages The great Trousseau is also said to have advised its exhibition in confluent smallpox and in malignant fevers With the quasi-experimental pharmacology of the time, the art of poisoning also developed considerably and Mithridates, king of Pontus, is reputed to have achieved a name in the art of giving and taking poisons He is said to have immunised himself against poisoning by drinking the blood of ducks fed on toxic principles and to have aspired to make a universal antidote

With Galen came experimental physiology and he revived the humoral pathology of Hippocrates His writings gave a new impetus to Empiricism But the Roman Empire was fast decaying and with it was falling the level of medical practice By the fifth century A D Aetius of Amida was treating his patients by incantations The saints of the Christian calendar took the place of gods of the savages and of the Greek temples This good Christian, Aetius of Amida, treated cases of foreign body, for example, a fish-bone in the throat, by repeating "As Jesus Christ drew Lazarus from the grave, and Jonah out of the whale, thus Blasius, the martyr and servant of God, commands 'Bone, come up or go down'" Or, Cato, the censor, reduced dislocations by repeating "Huat hunat ista pista sista domiabo damnaustra et luxato!"

After the fall of the Roman Empire the Arab or Moslem school of medicine (700—1096 A D) made many contributions to the progress of pharmacy The drug preparations—tinctures, confections, syrups, plasters, pomades, ointments—which they used were the best known to the practitioners, before the advent of modern inorganic and organic chemistry The writings of Razes (860—930) who described smallpox and measles so perfectly, were translated by Vesalius into Latin, and Avicenna

(980—1036) is said to be the first to describe the preparations of sulphuric acid and alcohol. He also recommended wine as the best dressing for wounds. The Mohamadan physicians used gilded and silvered pills and they prepared various syrups and elixirs. In search of the mysterious and the inexplicable they set out to discover the elixir of life and attempted the transmutation of metals. Naturally, they began to care more for alchemy than chemistry of drugs.

The most original thinker of the 16th century, Paracelsus (1493—1541) is said to be the precursor of chemical pharmacology and therapeutics. He attacked mysticism and witchcraft, he discarded Galenism and the four humours, and taught the physicians to substitute chemical therapeutics for alchemy. He made opium, mercury, lead, sulphur, iron, arsenic, copper and potassium sulphate a part of pharmacopoeia and wrote a book about the use of mercurials in Syphilis. He writes "Experience has shown that mercury is the sovereign and only remedy for the cure of all ulcers tainted with the great pox. Sublimated mercury is given by mouth, because its great virtue is known to everybody and it cures by inducing abundant expectoration of saliva."

The anatomical and physiological knowledge of the time was meagre and the theories of pathogenesis were fantastic, as will be seen from the following single extract from Cumston:

"The uterus was regarded as an animal which could be flattered and attracted by pleasant odours, while it disliked fetid odours extremely and attempted to escape from them. So Amatus Lusitanus in the 16th century treated uterine prolapse, as he thought, with considerable ingenuity, by causing his patient to inhale musk and pleasant scented herbs in order to attract the uterus upwards, while the vulva was exposed to the stench given off by galbanum and the smoke of burning feathers in order to cause the displaced organ to recede."

The therapeutics of the 16th and 17th centuries appear to be overshadowed by alchemy and various Cabalistic, Hermetic and Rosicrucian schools. In fact all the "six follies of science," namely, circle squaring, multiplication of the cube, perpetual motion, judicial astrology, alchemy, and magic were all rampant during these two centuries. Mindeier is said to have advised the plague doctors (during the Great London Plague) to repeat the twenty-second Psalm everytime they approached

a patient, just as the old Saxon Leschdoms urged the application of holy water and the intoning of Psalms LI and LXVII, over the cattle afflicted with pleuro-pneumonia

But in spite of all this darkness many doctrines of therapeutics—Borelli's Iatro-mechanism, Chemistry of Sylvius, Animism of Stahl, and Organic Dynamism of Hoffmann, were formulated during this time Borelli developed the iatro-mechanical doctrine, according to which all physiological and pathological processes could be reduced to shock, balancing, pressure and relaxation Sylvius formulated Chemistry in which chemical agents were preferably employed His doctrine attributed disease to acidity—which was either acid or alkaline and was treated by contrary medication Boerhaave (1668-1738), the founder of Electric school, whose writings were translated even into Turkish and Arabic and whose fame reached China, became the apostle of the iatro-mechanical theory He taught that there were three temperaments, salt, putrid and oily His treatments, which ought to have been tonic and stimulant, were rather depleting, and debilitating, and were selected from among purgatives, alkalies, sudorifics, dietetics and blood-letting, with a good dose of suggestion thrown in, because this burly man is said to have cured more patients by bullying and shouting than by drugs

We may just cast a glance in passing on the quaint drugs used during this time The first edition of the London Pharmacopoeia as published in 1610 contains 1,690 remedies, of which 1,028 were simples, 91 animal, 271 vegetable Among these were worms, lozenges of dried vipers, foxes' lungs for asthma, powders of precious stones, oil of bricks, oil of ants, oil of wolves, and butter made in May It also contained a Vigo's plaster, compounded of viper's flesh with live frogs and worms, and the celebrated antidote of Mattioli, made up of about 233 ingredients, including the *mithridate* and the *theriaca*. Among the queer remedies contained in the three pharmacopoeias (1618-1650-1677) of the century were the blood, fat, bile, viscera, bones, claws, teeth, hoof, horns, sexual organs, eggs, excreta of animals of all sorts, beeglue, cock's comb, cuttle-fish, fur, feathers, hair, human perspiration, saliva of fasting man, human urine (recommended by Madame de Sevigne, June 13, 1685, who also advocated the use of viper meat to temper, purify and refresh

the blood'), human placenta, snakes' skin, swallows' nest and wood-lice

With all its polypharmacy and fantastic organo and animal therapy, the seventeenth century introduced two drugs to the medical world for which at least, India will never forget it I refer to Cinchona and Ipecac And for the introduction of these, the medical world is indebted to the non-medical persons In the words of O W Holmes —

"Medicine learnt from a monk how to use antimony, from a Jesuit how to cure agues, from a friar how to cut for stones, from a soldier how to treat gout, from a sailor how to keep off scurvy, from a post-master how to sound the Eustachian tube, from a dairymaid how to prevent smallpox, and from an old market woman how to catch the itch-insect It borrowed acupuncture and the moxa from the Japanese heathen, and was taught the use of lobelia by the American savage" What more do we need to be humble when we remember that the father of our most important modern theory in pathogenesis was a Paris chemist, Louis Pasteur, and the man who gave us second eyes was a German physicist, Conrad Roentgen ?

About the year 1630, the Countess of CINCHON, vicereine of Peru, was cured of malarial fever at Lima by the administration of some bark, which had long been known to the Peruvians, and which was brought to Europe by the Jesuits in 1632 and later by Jaun de Vigo No other event, says Neuburger, did so much to upset the current systems of medicine as the discovery of Jesuits' Bark It is said that Cinchona did for medicine what gunpowder did for war IPECAC was brought to Paris by a Portuguese in about 1680 and was extensively prescribed as a secret remedy by Helvetius and at the instance of Louis XIV the secret was tried out and purchased by the French Government for 20,000 francs in 1688 The drug had since many ups and downs prior to the introduction of emetine in 1910 TARTAR EMETIC (antimony) first introduced in 1631, cured Louis XIV of some dangerous illness in 1657 and came in great vogue for some years Perhaps there are few drugs which were the subjects of such savage attacks and passionate eulogies as antimony was for some centuries

Before discussing the advent of rational therapeutics as a result of advances in scientific knowledge during the following centuries, which practically dethroned the Empiricism from its

supreme position, two more theories of therapeutics need mentioning, one, that of Broussais and the other, that of Samuel Hahnemann

Broussais (1772-1838) considered excitation as the only pathogenic agent, which was either too weak causing debility or too strong causing irritation. He thought gastro-enteritis as the basis of all pathology (as Cullen thought nearly everything a neurosis or Curveilheir, a phlebitis)¹. He believed that nature had no healing power and it was necessary to abort disease by active measures. To this end he adopted a powerful antiphlogistic or weakening regime, the main features of which were to deprive the patient of his proper food and to leech him all over his body. As many as fifty leeches were applied at once. Of the scarcity of leeches in Broussais' time, Baas records that in the year 1833 alone 41,500,000 leeches were imported into France and only about ten millions exported. Yet in 1824-25 two or three millions were sufficient to supply all demands. His student, Bouillard, was even moved to greater torrents of blood, adding blood-letting to leeching. The vigorous attack, based on statistics, of Louis (who first described apical tuberculosis and typhoid fever) checked this practice of excessive bleeding, and finally abolished it.

As a result of some experiments on his own person, Samuel Hahnemann (1755-1843) started the school of Homoeopathy, the main tenets of which may be formulated as, "first, that diseases or symptoms of diseases are curable by those particular drugs which produce similar pathogenic effects on the body, second, that the dynamic effect of drugs is heightened by giving them in infinitesimally small doses, which are to be obtained by carrying dilution or trituration to an extreme limit, third, the notion that most chronic diseases are only a manifestation of suppressed itch or Psora". Hahnemann, in spite of his infinitesimal drug bills died a millionaire in Paris in 1843¹.

With the beginning of the nineteenth century begins the modern era in medicine. Clinicians like Louis, Laennec, Bouillard, Corvisart, Pinfel of the French school, Graves, Stokes, Corrigan of the Irish school, Bright, Addison, Hodgkin, Carswell, Parkinson of the English school, Skoda of the Viennese school and others, put clinical medicine on a sound footing, and the sciences of Anatomy, Histology, Physiology, and Biochemistry made tremendous advances under men like Bichat, Claude Bernard, Johannes Muller, His, Carl Ludwig and others, and con-

nected up scientific medical knowledge with the bedside observations of the great clinicians of the age. This finally opened up the road to Rational Therapeutics.

Lauder Brunton, Sydney Ringer, Binz, Cushney and others applied physiological method to the study of drugs and applied a vigorous sifting process to the vast number of alleged remedies listed in the pharmacopoeia and put the use of drugs on scientific basis. After this Cushney pointed out that remedies may now be numbered in units where they were once counted in scores. The French clinicians Henri Huchard and Charles Flessinger, for instance, have limited actual drug therapy to some twenty remedies or groups of remedies, viz., opium, mercury, quinine, nuxvomica, digitalis, arsenic, phosphorus, ergot, belladonna, chloral, bismuth, the iodides, the bromides, the hypnotics, the purgatives, the antiseptics, the nitrites, the sera and vaccines, and the animal extracts each of which has a specific therapeutic action.

Besides this sifting of drugs, and finding physiological basis for their use, the last century saw intensive specialization in therapeutics such as electrotherapeutics, climatotherapy, hydrotherapy, dietetics, gymnastics, massage, hypnotism and many others which have reached a very high degree of perfection. In many ways this was a return back to the Hippocratic principles of nature therapy, and the movement may be taken as a beginning of the neo-hippocratic period.

In 1845, Rynd introduced the hypodermic syringe and the subcutaneous method of introducing drugs. 1846 saw the most important therapeutic discovery of all ages. Morgan, a Boston dentist, discovered ether and introduced it in surgical practice. In the following year, 1847, Simpson introduced chloroform as an anaesthetic at Edinburgh. Louis Pasteur (1822-1895) and Robert Koch (1843-1910) founded the science of bacteriology which completely transformed the ideas about the pathogenesis of disease. A new pathology and a new medicine was the outcome of the work of Louis Pasteur, the great chemist of Paris. Lister, following Pasteur, gave his antiseptic method to the world in 1866 which together with ether and chloroform, completely transformed the practice of surgery. As the science of bacteriology developed sero-therapy and vaccino-therapy, for which we are indebted to Roux and Von Behring, Metchnikoff and Wright, were added to the rational therapy. Ehrlich (1854-1915) introduced chemotherapy with his salvarsan, in 1910 an ideal *therapia*

sterilisans in case of spironema, and added a new territory to the domain of experimental pharmacology and therapeutics

The last quarter of the nineteenth century and the first quarter of the twentieth century may be considered as an era of therapeutic nihilism or helplessness—the era of Osler, who was the master exponent of the therapeutic helplessness of his generation. The art of diagnosis with the help of the ancillary sciences, x-rays, biochemistry, bacteriology, and the electrocardiogram, reached a high degree of perfection. Clifford Allbutt said a physician could hope to make a correct diagnosis in as many as 70 per cent of his cases. The Vienna school vied in the ability to make a correct diagnosis at the bedside and to verify it successfully in the post-mortem room. But during the interval from the bedside to the post-mortem room no active help was given, except perhaps a sympathetic understanding with which the patient was watched to proceed to recovery or death. Patients were admitted in the wards, endless questions were asked, thorough physical examinations were repeatedly made, and investigations of all sorts were carried out until a clear picture was obtained of the morbid anatomy but nothing was done about treatment. The aim of a practising physician is to help his patient to recover but the physicians of this era were helpless. They discarded the false beliefs of the past ages but had not developed any new ideas in treatment. Osler said in 1902, "In the fight which we have to fight incessantly against ignorance and quackery among the masses, and follies of all sorts among the classes, *diagnosis not drugging*, is our chief weapon of offence. The salt of life for the physician is a judicious scepticism, not the coarse, crude form, but the sober sense of honest doubt expressed in the maxim—Be sober and distrustful, these are the sinews of the understanding."

A new era in therapeutics dawned with the replacement of the post-mortem view of medicine by the functional or the physiological view. The question asked was: How has the body reacted to the new environment? How is the function affected and how can it be altered? The conception of *hormones* as pharmacodynamic bodies, the discovery of *vitamins* acting not as mysterious minute agents but as pure chemical bodies which can be synthesised and weighed in the laboratory, the conception of the deficiency diseases, the discovery of the erythrocyte maturing factor in the liver, the production of a number of drugs regulating the autonomic nervous

system, the extension of the chemotherapy by the discovery of the sulphomide and the amidine group of drugs, and the transfusion of gum acacia, hypertonic salts, whole blood, serum, plasma or cells,—have opened up new vistas in the therapeutic fields which make the practice of medicine at the present time really worthwhile both for the physician and his patient

In 1884, Victor Horsley produced artificial myxoedema in a monkey by thyroidectomy and Kocher about the same time did the same in a human subject, which initiated the study of ductless glands. The therapeutic use of thyroid extract in cretins and myxoedema opened up a new branch of rational therapeutics—that of substitution opotherapy. Isolation of adrenalin in 1901 by Takamine from the suprarenal gland and its physiological study by Elliott extended the domain of opotherapy in therapeutics. And in recent times the isolation of thyroxin by Kendall and insulin by Banting and Best, and parathyroid hormone by Collip, various pituitary hormones, suprarenal cortin, testosterone, estrogenic hormones, and corpus luteum hormone, has greatly extended the scope of organo-therapy.

Finally, a word about vitamins, for which we are indebted to Hopkins and Mellanby. The discovery of these made clear the pathogenesis of certain general diseases, now known as deficiency diseases and which are cured by the timely exhibition of appropriate vitamins.

Of recent years the work of Kraepelin, Freud and Jung is also introducing order into the chaotic therapeutics of psychiatry, putting it on a rational basis. The shock and convulsions produced by insulin and cardiazol have given new hopes of recovery in hopeless cases of schizophrenia and depression. The malarial and other fever therapy has altered the prognosis of general paralysis of the insane.

This rather cursory survey of the evolution of rational therapeutics may well be closed with the words of Cumston, a modern medical historian and philosopher—"That great mind of the Renaissance, Francois Rabelais, once said that the practice of medicine is but a farce played by three actors, the physician, the patient and the disease. It may have been so once, today the practice of medicine is an Empiricism tempered by science, a growing Rationalism—an Empiricism that will become more and more scientific if only the enthusiasms of the moment are corrected by the philosophy and judgment that nothing but a knowledge of the History of Medicine can supply."

Society Proceedings

SETH G S MEDICAL COLLEGE STAFF SOCIETY

The 24th meeting of the Seth G S Medical College Staff Society was held on Saturday the 13th March, 1943 at 2 p m (S T) in the K E M Hospital Prof S P Niyogi presided Dr V N PATWARDHAN read a paper on

VITAMIN D AND RICKETS

Funk in his book on vitamins published in 1914 mentioned the possibility of rickets being a deficiency disease A few years later Mellanby (Med Res Council, Special Report, Nos 38 and 61, 1919 and 1921) was successful in producing rickets in puppies kept on a diet of separated milk, white bread, linseed oil, yeast, orange juice and NaCl This was undoubtedly the first important investigation of rickets from an experimental standpoint Mellanby demonstrated beyond doubt that cod liver oil only of all the fats was useful in curing rickets He ascribed the curative action to the vitamin A of the cod liver oil Two or three years later McCollum and his associates showed that the cod liver oil contained two fat soluble vitamins, one was vitamin A then already known and the second was the antirachitic factor named by him vitamin D

Since then intensive research work has brought to light several forms of vitamin D (Bills, Jour Amer Med Assoc 108, 13, 1937) Of these only two are of practical importance, while the others remain as chemical curiosities Calciferol or vitamin D is obtained by irradiation of ergosterol and represents the synthetic product Vitamin D₃ is obtained by the irradiation of 7-dehydro-cholesterol and is believed to be the naturally occurring vitamin The antirachitic potency of both of these as measured by the rat assay is 40,000 I U per milligram Rat unit per rat unit, calciferol is about 1/100 as active as vitamin D in curing rickets in chickens In human beings the difference between the antirachitic potencies of these two vitamins is rather small, i.e., 1.15 or thereabout The problem of the difference in potency of these two vitamins is not

tary tract in the various digestive secretions, most of it is normally absorbed. The amount of calcium and phosphorus found in the faeces is then probably the sum of the quantity left unabsorbed from the diet as well as from digestive secretions and that excreted into the intestines. Hence, although the balance method might yield useful information about the total retention of calcium and phosphorus it will not give a true picture of absorption alone. Recently, however, the isolated loop technique of Verzář has been used by Nicolaysen (Biochem J 31, 122, 1933) and Laskowski (Biochem Zeitschr 292, 319, 1937) for studying the absorption of inorganic phosphate, glycerophosphate and calcium salts from intestines. Nicolaysen's results showed that in absence of vitamin D the absorption of calcium from the intestinal loops was decreased. On a close scrutiny of his work some faults in technique and fallacies in argument were found. It was decided, therefore, to carry out fresh experiments on albino rats.

The rats chosen for experiment were starved for 18 to 20 hours before they were used. The isolation of the loop was performed under ether narcosis. The accurate measurement of the length of the loop *in situ* was very difficult, hence, as far as possible the entire length of the small intestine from pylorus to the caecum was isolated by ligatures at both ends. Small glass cannulas were passed in at these ends and the lumen washed carefully with 100 c c to 125 c c of warm physiological saline solution made in glass-distilled water till the washings were free from calcium. This fluid was gently pressed out between two fingers. The ends were then tied off and the cannulas removed. 2 c c of solution of calcium gluconate containing 12.3 mg of calcium were injected into the intestine near the pyloric end of the ligated loop by means of a syringe fitted with a very fine needle. The loop was then replaced in the abdomen, the walls closed, sutured and the narcosis discontinued. After three hours, the rats were killed by chloroform, the loops removed and the length measured. A glass-cannula was passed from one end and the loop was washed with glass-distilled water till the washings were again free from calcium. This required about 150 c c to 175 c c of water. The washings were acidified, made to volume and the calcium estimated.

To ascertain the accuracy with which calcium gluconate solution could be delivered by the syringe, several trials were carried out in which 2 c c of the solution were delivered into different beakers and the amount of calcium estimated. The results showed that the delivery from the syringe was quantitative and uniform. It was also essential to find out if all the calcium introduced into the intestine could be quantitatively recovered. For this purpose, six rats were used in which the loops were washed immediately after introducing the calcium salt. The estimation of calcium in the washings proved that it could be recovered almost quantitatively (98.63-2.22) per cent.

The normal, hypervitaminotic and rachitic rats and those protected from rickets by vitamin D were employed for the investigation. Young rats were rendered rachitic by feeding them a rachitogenic diet, a second group which was also kept on a similar diet was protected by a dosage of 60 I U of vitamin D per rat per day. A third group was maintained on the stock diet of the colony. In addition to these some rats bred from stock receiving vitamin D poor diet and continued on a similar diet after weaning were utilized (Patwardhan and Chitre, *Ind Jour Med Res* 30, 81, 1942).

TABLE I (12.3 mg Ca introduced)

		Mg Ca absorbed in 3 hours	Ca mg cm loop	
A	Rats on stock diet	4.86 ± 1.20	0.133 ±	0.030
B	4 rats on stock diet + 7200 I U vit D for 4 days	3.76 ± 0.596	0.105 ±	0.018
C	5 rats on stock diet + 7200 I U vit D per rat per day 30-60 days severe hyper- vitaminosis	4.16 ± 0.847	0.116 ±	0.063
D				
	8 rats on rachitogenic diet	5.63 ± 1.66	0.165 ±	0.01
	5 rats -do- + 60 I U per day	6.14 ± 2.27	0.199 ±	0.082
	5 rats on stock diet	4.21 ± 1.24	0.117 ±	0.030
	7 rats on vit D deficient diet	3.96 ± 0.567-	0.097 ±	0.015
	6 rats -do- + 60 I U per day per rat	4.10 ± 0.896	0.090 ±	0.018-

These experiments leave no doubt as to the fact that vitamin D has no direct influence on the absorption of calcium from the intestines of the rats. In view of the fact that the supporting evidence about the supposed effect of vitamin D on calcium absorption in clinical rickets was derived from experi-

ments on rats, the results reported here can be said to apply to human rickets as well

So far as the absorption of phosphate is concerned there was not much doubt that it was also uninfluenced by vitamin D. Further proof, if any, was needed, has been supplied by Moigareidge and Manley (*J Nut* 18 411, 1939) with the use of radioactive phosphorus. In view of these findings it becomes necessary to find a satisfactory explanation for the increase in the faecal calcium and phosphorus in vitamin D deficiency usually observed clinically as well as in experimental animals. It is suggested that although vitamin D may not exert a direct influence on the absorption of calcium and/or phosphate it is possible that it may do so indirectly by altering the condition or conditions in the alimentary tract which in a normal animal are not unfavourable for the absorption of these elements. It must be borne in mind that the experiments described above have been carried out with calcium salts alone in absence of any extraneous disturbing factors. It is known, however, that pH of the tract and its contents, quantity of fats in the diet, the ratio of Ca/P, etc., are some of the factors which might determine the extent of absorption. Although, considerable work has been done on this question by various workers, it has not been conclusive. Any accepted hypothesis of vitamin D action will have to explain satisfactorily the relation between the state of vitamin D deficiency and large faecal excretion of calcium and phosphate.

Thus having convinced ourselves that vitamin D did not act by directly influencing the absorption of Ca and P from the intestine we proceeded to investigate the effect if any which vitamin D had on the concentration of Ca and P and other substances in the blood. The reason for this step is not far to seek. Any change which results in improved calcification of the bone must be primarily sought for in the plasma which is the fluid influencing the immediate environment of the bone cell. We analysed a number of blood samples obtained from children through the courtesy of the authorities of Bai Jerbai Wadia Hospital for Children. We also followed at the same time the progress of the rachitic state and its healing induced in dogs kept under controlled conditions and tried thus to confirm the findings of investigations on rachitic children. A

broad outline of procedure given here will be helpful in following the discussion

Experimental Rickets

These experiments have been carried out over the last three years. Each year in the month of May a batch of 4 or 6 young puppies 3-4 weeks old was selected for experiments. They were fed vitamin D deficient diet made up as follows —

Rice	152 gms
Bread	114 gms
Skim milk	370 c c
Meat	43 gms
NaCl	2 gms

Each batch was divided into 2 groups one serving as a control. The diet of the latter was supplemented with 400-600 I U of vitamin D as a protective measure. Both the groups received adequate quantities of vitamins A, B (Complex) and C, in the form of red palm oil, yeast extract and ascorbic acid. Blood was removed from each dog once a fortnight by puncture of external jugular vein. X-ray photographs of the distal ends of the radius and ulna were taken once a fortnight or once a month as was thought necessary.

The following determinations were made on the blood serum: (1) calcium, (2) acid soluble phosphorus (total and inorganic), (3) magnesium, (4) total protein, albumin and globulin, (5) chloride, (6) total base and occasionally, (7) non-protein nitrogen. The pH was determined on the whole blood, and in some cases haemoglobin also was estimated.

When the state of vitamin D deficiency had progressed for three to four months, vitamin D was administered orally in doses of 2,000 to 5,000 I U per day per dog. The experiment was stopped when there was no further radiological evidence of deficient calcification at the epiphyses.

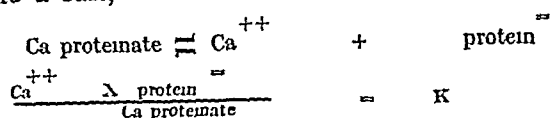
In the first batch of 6 dogs, three of which were receiving vitamin D deficient diet, none developed rickets which could be radiologically or histologically proved. This negative finding has also some importance to which reference will be made later. In the second batch, two out of three experimental animals developed rachitic epiphyses while all the three control animals showed normal epiphyseal ends. In the third batch, one out of two developed typical rickets, controls did not show any abnormality.

It must be pointed out that in higher animals like dogs and monkeys it is very difficult to produce uniform experimental lesions of any given type in all animals of a batch even though the animals are kept under identical conditions. Why it is so still remains unexplained. On the other hand in animals like the rat much greater uniformity of response can be obtained. If this is conceded one can claim a reasonable measure of success in the experiments outlined above.

The most noticeable change was in the calcium and less so in phosphorus of serum. The other constituents did not show any appreciable change with the progress or the cure of the disease. In the second batch of dogs the calcium content of serum progressively decreased till the difference between the control and rachitic group was 1.5 mg p.c. The difference did not increase further. The calcium rose after administration of vitamin D, and Ca levels in both the groups approximated. In the total protein as well as in albumin and globulin there has been no appreciable change during the whole experiment. This observation itself is significant as explained below.

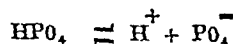
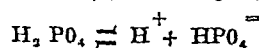
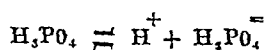
The protein which is present in blood, whether it be in the plasma or corpuscles, acts as a weak acid combining with a certain amount of base. In plasma, part of the calcium exists in such a combination with protein (Schmidt and Greenberg, *Physiol Rev* 15, 297, 1935). The calcium which is not protein-bound is diffusible. Thus, it will be clear that calcium exists in blood in two forms—diffusible and non-diffusible, the whole of the non-diffusible portion being in combination with protein. The remaining portion is diffusible and most of it exists in ionized state. On this ionic form of calcium depend, some of the functions of calcium, *viz*, irritability at the neuro-muscular junction, tone of the plain muscle, membrane permeability, etc. In low calcium tetany it is believed that it is the ionized fraction that is diminished. Hence, the maintenance of the proper level of ionized calcium should be considered as more important than the maintenance of total calcium level. Although parathyroid glands are believed to control this function, it is not known how they do it. The protein content of plasma or serum has a direct influence on the concentration of ionized calcium. If the former is decreased or increased, there must be a simultaneous change in the same direction in the level of total

serum calcium The relation has been expressed by McLean and Hastings (Amer Jour Med Sci 189, 601, 1935) mathematically by Mass Law equation Assuming that calcium proteinate would dissociate like a salt,

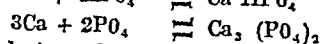
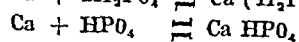
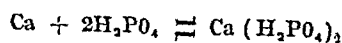


Thus if the total calcium and total proteins of the serum are known Ca^{++} concentration can be easily calculated McLean and Hastings have prepared a nomogram reference to which gives the values of $[\text{Ca}^{++}]$ It has already been mentioned that in the experiments on dogs a decrease in total calcium as compared with the control animals was recorded, although no similar decrease in the protein or any of its fractions could be demonstrated This results, therefore, in a decrease of $[\text{Ca}^{++}]$ as calculated Attempts were made to confirm this finding by frog heart method But the experiments did not succeed owing to some technical difficulties

The inorganic phosphate of the serum can be estimated with accuracy and concentration of PO_4 in serum can be arrived at by calculations based on the laws of dissociation Thus, H_3PO_4 can dissociate in solution in three types of ions



The relative concentration of these three ions will depend upon the ionic strength of the serum and upon the $[\text{H}^{+}]$ of the solution or its pH which in case of blood is 7.35 to 7.4 and which was found to remain unchanged in rickets When $[\text{Ca}^{++}]$ are also present at the same time in the serum there will be equilibria between



At the pH of blood it is the CaHPO_4 that should be present in appreciable quantities While this work was in progress Freeman and McLean (Arch Path, 32, 387, 1941) published results of experimental rickets in which they observed that the ionic products of one of the calcium salts in blood decreased in experimental rickets

A few words seem to be necessary to explain the conception of the ionic product. An electrolyte in solution dissociates in ions, e.g., $\text{CaHPO}_4 \rightleftharpoons \text{Ca}^{++} + \text{HPO}_4^{--}$ and there then would be an equilibrium $\text{Ca}^{++} \times \text{HPO}_4^{--} = K \text{ CaHPO}_4$.

In saturated solutions the equilibrium can be written as
 $\text{Ca}^{++} \times \text{HPO}_4^{--} = K \text{ CaHPO}_4 \text{ (in solution)}$
 \downarrow
 $\text{CaHPO}_4 \text{ (solid)}$

In dilute solution the electrolyte is completely dissociated. Since CaHPO_4 is slightly soluble in serum it will be completely dissociated and there will be no undissociated salt in solution. If the product of $\text{Ca} \times \text{HPO}$ exceeds solubility product, the salt will precipitate. Similar considerations can be shown to hold in case of $\text{Ca}_3(\text{PO}_4)_2$.

The value of the solubility product of CaHPO_4 expressed as its negative logarithm found by investigators working on salt solutions made up similar to the composition of serum varies between 5.47 and 5.6 (Logan, *Physiol Rev*, 20, 522, 1940). In other words, if the values of pK s p CaHPO are found to exceed these figures the serum would be undersaturated with respect to the salt. On the other hand, lower values would indicate these figures the serum would be undersaturated with respect to the salt. On the other hand, lower values would indicate that the serum is supersaturated and the conditions favourable for bone deposition. Similar considerations apply in case of Ca_3PO_4 . The $\text{pK s p Ca}_3(\text{PO}_4)_2$ is 23.0.

The calculation of our figures according to these methods showed that in experimental rickets the values for vitamin D deficient animals indicated undersaturation of serum with regard not only to CaHPO_4 but also with regard to $\text{Ca}_3(\text{PO}_4)_2$.

Clinical Rickets

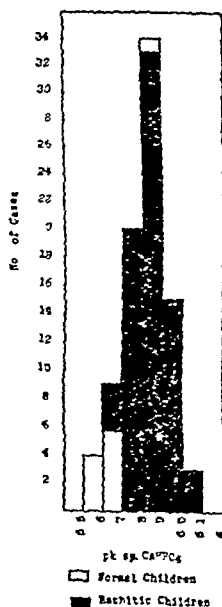
Dr R. N. Cooper kindly allowed us to collect samples of blood from Bai Jerbai Wadia Hospital and through the help of Dr Adenwalla it was possible to get a good number of blood samples. In the earlier part of the investigation, the clinical diagnosis of rickets was the only criterion, applied before collecting the sample of blood. Later, it was decided to take blood and an x-ray picture of the wrist joint of every child suspected to be rachitic. The amount of blood required was between 7 and 10 c.c. and it was not always possible to obtain the required

quantity with the result that several samples could not be fully analysed. All the constituents of serum or blood which were investigated in experimental rickets were also estimated in children's blood. Complete data with x-ray pictures, but not always the clinical history, are available for 40 cases of suspected rickets. Of these, 30 show radiological signs of rickets. The severity of the lesion was kindly interpreted by Dr Z J Joseph to whom the author is grateful. The remaining 10 cases did not show any evidence of rickets radiologically. Some blood samples of children termed the hospital normals have also been obtained. Further with the permission of the Superintendent of the J J Group of Hospitals and the kind co-operation of Dr Coelho, some blood samples were also obtained from the B J Hospital for Children. The figures for these are also included in the chart.

The results in these cases followed a similar trend as in case of induced rickets in dogs. Apart from the decrease in Ca and/or P no other constituent could be shown to have suffered materially due to the onset of the rachitic condition. The considerations outlined above, about the reaction between total Ca and protein of serum hold in these cases as well. A fall in $[Ca^{++}]$ (as calculated) has been observed in serum of rachitic children.

McLean and Hastings have observed that in clinical rickets the $[Ca^{++}]$ does not decrease, an observation which our findings do not confirm. The decrease must ultimately result in undersaturation of the serum of rachitic children with regard to the calcium salts taking part in bone formation. The chart on the right side, shows quite well the state of saturation or otherwise of blood serum of rachitic and normal children.

A scrutiny of the interesting chart reveals the fact that there appears to be a sharp demarcation between normal and rachitic children. The value for only two of the rachitic children appears to indicate supersaturation, in one of these Ca and P



were also high, the x-ray appearance was normal and in the other no x-ray picture was available. Another fact which emerges from this is that those cases which were diagnosed by the clinician as rachitic but in whom the epiphyseal changes could not be seen radiologically are also found on the rachitic side in the chart, thus vindicating the diagnosis of the clinician. It is felt, however, that the number of cases is yet too small, especially the normals, to enable me to draw far reaching conclusions. I would not have ventured to draw even these conclusions, had it not been for the confirmatory evidence obtained in controlled experiments on rickets in puppies as already described.

It has been mentioned earlier that in the first experimental batch the dogs did not develop rickets, yet the values for the ionic product diverged from those of the control animals in such a manner as to indicate a definite vitamin D deficiency. In the second and the third batches some animals developed typical rickets and also gave evidence of undersaturation. The latter was remedied by administration of vitamin D, the ionic product improving much before the return of the epiphyses to the normal. This brings us to a very important and interesting question of diagnosis of early rickets or the pre-rachitic condition. Either of these may be of little importance to the clinician but if allowed to develop unchecked may well become serious. Further, one must not forget that a prolonged but mild deficiency of vitamin D may seriously affect the growth of the individual. The amount of vitamin D required for good growth is more than the quantity required to prevent the onset of rickets. Thus the problem of the diagnosis of early rickets and the pre-rachitic state is of importance to the clinician as well as to the nutrition worker.

The knowledge of the occurrence of some chemical changes in blood accompanying the development of rickets has been utilized from time to time for suggesting methods for chemically diagnosing the disease. Two conditions must be fulfilled before such diagnostic methods can be said to be successful (1) The change must be specific and (2) it must take place before the clinical signs appear, otherwise the chemical diagnosis will be only of a confirmatory nature or even superfluous. The two or three diagnostic procedures suggested during the

last 20 years and used for varying lengths of time and with varying success were $\text{Ca} \times \text{P}$ product, serum inorganic phosphorus, and plasma phosphatase. Howland and Kramer in 1921 put forward the suggestion that a $\text{Ca} \times \text{P}$ product below 30 indicated active rickets. Later on, so many exceptions to this rule were found that this method had to be abandoned as a diagnostic measure. The other to be considered was the serum inorganic phosphorus which showed decrease in rickets. It has been observed by many that the fall is usually not significant until after the disease is noticeable by clinical signs. Besides, one might point out that low serum phosphate is not a uniform finding in rickets which further detracts from its value. The next to enter the field was the plasma phosphatase. The rise in plasma phosphatase in rachitic children is greater than in other diseases and is said to set in early. Barnes and Carpenter (*Jour Pediatrics*, 1937) compared the diagnostic procedures based on (1) radiological findings, (2) fall in serum inorganic phosphorus and (3) increase in plasma phosphatase. They report that out of a total of 187 cases 25 p c could be diagnosed by radiological examination, 20 p c by the serum inorganic phosphorus and 65 p c by the plasma phosphatase. There is no doubt, therefore, that a large measure of success can be achieved by applying the phosphatase test in diagnosing the condition of early rickets. It cannot be denied, however, that it still leaves an appreciable proportion of cases undiagnosed. Further, it must be remembered that the plasma phosphatase rises in hyperparathyroidism, Paget's disease, osteomalacia, carcinoma with osteoplastic metastases to bone and in some cases of osteogenic sarcoma. The elevation of plasma phosphatase in such diverse conditions can hardly be taken as a specific indication of vitamin D deficiency. (Morris and Peden, *Quart J Med*, 6, 1937.)

This leaves us the diagnosis of rickets on clinical findings alone aided sometimes by x-rays. Hess (*loc cit*) has reported his own observations on 51 infants in his clinic throughout autumn, winter and spring where a comparative study of the earliest signs of rickets was made. Generally, beading of the ribs preceded a definite fall of phosphorus, in some instances the reverse was true. Roentgen rays were found of limited value the lesions becoming apparent by radiographs, some

weeks after the beading of ribs or the decrease in the blood phosphate. Similarly, Wimberger (quoted from Hess) says that 'from investigation of post-mortem material in which Roentgen ray pictures and histological sections were made from one and the same bone, it was found that the interval of time between the first histological rachitic change and the first radiographic change is certainly as long as several weeks'. Besides one need not lose sight of the fact that craniotabes, beading of the ribs, diminution of the serum phosphorus, increase of plasma phosphatase, the characteristic epiphyseal changes, etc., are not indications of the early stage of rickets but that all of these should be regarded as the result of a rachitic disturbance which has existed for weeks or even months in the cells and tissues.

In support of the plea for a trial for the ionic product as a diagnostic measure the following few facts may be considered relevant.

- 1 The rachitic cases so far investigated, whether radiologically positive or negative, showed definitely a state of undersaturation with respect to CaHPO_4 and $\text{Ca}_3(\text{PO}_4)_2$.

- 2 Several rachitic cases were encountered where the calcium and phosphorus of blood serum were either normal or high. In some x-rays showed well developed rickets. In spite of high Ca and/or P the ionic products in these cases showed undersaturation. There should be no difficulty of diagnosis of such cases when the clinical picture must be well developed, but cases with high Ca and P and in the stage of incipient rickets can be diagnosed by the ionic product method.

- 3 In experimental rickets it was observed that the ionic product indicated the deficiency of vitamin D even before a marked fall in Ca or P of serum had set in.

- 4 Although it is true that from the data available till now, no relation can be established between the severity of rickets and the extent of undersaturation, the possibility must be investigated.

Taking all these things in consideration it is felt that this test for diagnosing vitamin D deficiency and early rickets merits a fair and extensive trial both at the hands of the clinician as well as workers interested in problems of nutrition.

Discussion

(1) Dr Kurulkar asked whether correction for small samples was applied in the statistical treatment of the data on absorption.

(2) Dr N A Purandare wished to know if the plasma phosphatase rise was accompanied by increase in calcium and inorganic phosphorus of the serum. He, further observed, that clinically one seldom found a picture of undiluted vitamin D deficiency. The infant or the child showed signs of vitamin A deficiency as well. As the absence of vitamin A is known to cause keratinisation of the epithelium, the faulty absorption of calcium and phosphorus observed in rickets may be due to the abnormal condition of the intestinal mucosa.

(3) Dr Dhurandhar wished to know what part the parathyroids played in altering the metabolism of calcium in rickets.

(4) Dr Khanolkar said that he had observed an increase in the plasma phosphatase in several cancerous patients. He asked the speaker whether any work had been done on the ionic product of CaHPO_4 in such cases.

(5) Dr Raghavan observed that the increase in the serum concentrations of calcium and phosphorus after vitamin D administration must be due to increased absorption from the intestine.

In reply Dr Patwardhan clarified certain points raised in the discussion. (1) As the number of animals used in the experiments was small the data were always treated statistically and corrections for small samples were also applied. (2) A rise in the serum calcium and phosphorus accompanying increased plasma phosphatase in rickets was not known to occur. (3) The faulty absorption of calcium in rickets could not be ascribed to keratinisation of epithelium due to superadded vitamin A deficiency for the reason that on treatment with pure vitamin D only the faecal calcium showed a decrease. (4) What part the parathyroids played in rickets was not known. In low calcium rickets a hyperplasia of parathyroids had been observed, but this was not a constant finding in all cases of rickets. (5) It is not correct to assume that increased levels of serum calcium and phosphorus on administration of vitamin D were due to increased absorption from the intestines. By suitable experiments it can be shown that the serum calcium increased on administration of vitamin D even when the animal had received no calcium in the diet.

Professor Niyogi observed as follows in summing up the discussion on the three main findings of the lecturer, viz —

- (1) Vitamin D does not influence absorption but it helps the retention of Ca.
- (2) In rickets there is a correlation between calcification and solubility product of Ca and Po_4 ions.
- (3) The ionic product test is capable of application for diagnosing early ricket and early stages of vitamin D sub-nutrition.

(1) In spite of the extensive amount of work that has been done on the role of vitamin D in the maintenance of Ca and P levels of blood, no satisfactory explanation can be given as to the cause of decrease of Ca or inorganic P in blood in experimental and clinical rickets. Whether the decrease is due to reduced absorption or

enhanced excretion cannot be definitely stated at present owing to divergence of opinion among different investigators all of whom have put forward definite experimental evidence in support of one view or the other. This lack of precise knowledge is probably the reason why Park in a recent issue (1940) of *Journal of American Medical Association* has expressed the view that 'No one knows how vitamin D acts'

(ii) The finding that in rickets there is a definite correlation between the solubility product of Ca and PO_4 ions and calcification cannot be reconciled with certain well known physiological facts. In a rachitic animal it is perhaps possible to raise the ionic product to the saturation level by the administration of Ca and parathormone but there may not be any calcification in the absence of Vitamin D, parathormone cannot certainly be substituted for Vitamin D in the treatment of rickets. In rickets the phosphatase activity of the plasma increases but in the blood percentage of phosphoric esters hydrolysable by phosphatase does not fall below normal, on the phosphatase hypothesis there is, therefore, a possibility of PO_4 ions increasing with the progress and severity of the disease and the ionic product reaching the saturation or supersaturation level but as a matter of fact no calcification occurs. With the discovery of phosphatase it has become impossible to explain ossification on the ionic product concept, for calcification does not appear to be a question of simple precipitation of Ca and PO_4 ions from a saturated or supersaturated solution, the activity of living cells is also concerned in the process and vitamin D perhaps exercises some unknown influence on this activity. The trend of recent work indicates that vitamin D has a dual role in calcification. It probably maintains the ionic product of Ca and PO_4 of blood at a particular level and at the same time it exerts a specific effect on osteoblasts and cartilage cells permitting the utilization of these ions in the process of ossification.

(iii) Professor Niyogi fully agreed with Dr Purandare's views regarding the rise of plasma phosphatase in the very early stages of rickets. The method of estimation of the enzyme is quite simple and straightforward and the enzyme content of the plasma does furnish a reliable help in the diagnosis of latent and active rickets. The rise of plasma phosphatase is more well marked in rickets than what is found in some other diseases of bony skeleton which affect infants and young children. It is not the mere rise but the actual extent of the rise that gives the diagnostic indication in rickets. In view of the simplicity and reliability of the phosphatase test it may not be possible to replace it by the ionic product test so far as clinical work is concerned.

Critical Notes and Abstracts

NICOTINIC ACID IN ACNE VULGARIS

Use of nicotinic acid in the treatment of acne vulgaris in forty-six students at the University of Minnesota is described by F W Lynch (*Arch Dermat, & Syph* 42 481, 1940) The patients had received no previous treatment for at least three months preceding the use of this preparation Nicotinic acid was administered twice daily in the form of 50 mgm tablets taken after the morning and the evening meals No other treatment was used and the students were given no advice concerning diet or hygiene The only unpleasant reaction observed was transitory redness, burning, or itching in the flush areas of the face, chest and arms This reaction was avoided if the drug was taken immediately after meals

Eight of the forty-six patients failed to present themselves for re-examination The remaining thirty-eight patients were examined in three or four weeks and again in six to eight weeks In six (16 per cent) the results were classed as good and in fifteen (39 per cent,) as fair, in seventeen (45 per cent) no improvement was noted

While Lynch does not believe that nicotinic acid should be regarded as a cure for acne, he states that it is a simple and apparently harmless drug which seems to help in the treatment of this condition He points out that there may be some relation between nicotinic acid and the metabolic requirements of the staphylococcus The influence of the drug on the seborrheic oiliness was most striking

NICOTINIC ACID IN ANGINA PECTORIS

F J Neuwahl (*Lancet*, 2 419-Oct 1942) treated 6 patients suffering from angina pectoris with niacin and the results appeared to be remarkably uniform and lasting Oral administration of the drug caused a noticeable decrease in the number and the severity of attacks in several patients, in others the effect was transient, possibly because absorption or interaction of chemical substances in the gastric secretion was interfered with Intravenous administration heightened the efficacy of the drug Therefore, to obtain equal conditions oral administration was discontinued and a drip infusion of a 0.05 per cent solution of niacin was chosen to overcome differences in susceptibility One infusion of 100 to 300 mgm of niacin produced as a rule a remarkably beneficial result, which was maximal after twelve to twenty-four hours Further, infusion seemed to cause a definite stabilization in the condition of the patients, who became free from anginal attacks after several weeks The worst affected patients reacted best Usually, six infusions were sufficient The symptoms of the 6 patients have completely or almost completely regressed from three to seven months after the

course of treatment was completed, 3 have actually resumed heavy manual work

CHARACTER OF CONGESTIVE FAILURE IN CHILDREN WITH ACTIVE RHEUMATIC FEVER

The clinical features of congestive failure in children with rheumatic fever are described by B J Walsh and H B Sprague (*Am J Dis Child* 61 1003, 1941), their observations being based on a study of forty-four children between the ages of 3 and 15 years

The initial signs of heart failure in these forty-four children with rheumatic fever and congestive failure were enlargement of the liver and puffiness of the face accompanied by unexpected gain in weight. A few children with congestive failure and active rheumatic fever preferred to lie flat in bed. These children had marked puffiness of the face, which caused them to look as if they had primary renal disease

Pulmonary rales were seldom heard in these children, their appearance being limited to the terminal stages of the illness

Other important evidences of congestive failure in children with rheumatic fever and congestive failure were high venous pressure apparent at the onset of the failure, a shift of the electrical axis of the heart to the right, which increased with progression of the heart failure and decreased or disappeared with the patient's improvement or recovery, and a well marked diastolic gallop rhythm along the upper left sternal border

THE ACTION OF DRUGS ON THE CALIBRE OF CORONARY VESSELS

(Linder, E and Katz, I *N Jour Pharm & Exper Therap* 72 306, 1941)

The digitalis derivatives, K-strophanthin, ouabain and digifoline have a direct coronary constrictive action even in therapeutic doses

Metrazol and glucose are mild, direct coronary dilators

Calcium gluconate, in contrast with the chloride salt which is a powerful dilator of the coronary vessels, does not cause any constant or striking change in coronary calibre, except that a mild dilatation occurs with large doses

Aminophyllin and caffeine sodium benzoate are consistently direct coronary dilators, the aminophyllin being the more powerful

Papaverine hydrochloride is a powerful long-lasting coronary dilator. Its action is direct. This and its tendency to prevent ventricular fibrillation probably explain its clinical benefits

ACTION OF CALCIUM ON HUMAN ELECTROCARDIOGRAM

Clarke, N E has studied the action of calcium on the human electrocardiogram in four subjects. He used a 2 per cent solution of calcium chloride by vein, the dose being 40 to 75 grains. He concludes that the intravenous therapeutic use of calcium has advantages and benefits, but carries definite danger

Calcium produces changes in the human electrocardiogram which are progressive and depend upon the calcium concentration in the blood stream

The earliest and vagus-like actions are bradycardia, sinus arrhythmia, shifting of the pacemaker, and various degrees of heart block

Calcium may act directly upon the ventricular muscle, increasing its excitability and producing foci of idiopathic ventricular rhythm and ventricular extrasystoles of large and unusual form

(These actions of calcium may prove extremely alarming and even fatal in the presence of digitalisation N D P)

The blood-pressure was altered, the systolic level being raised and the diastolic depressed. Accompanying psychic factors and symptoms such as nausea and chest oppression, could account for some of the change

The author observed no diuresis from calcium administration and the effects on the heart were very transitory

THE SPRUE-SYNDROME

F M Hanes discusses (Amer, J Med Scien Sept 1942 p 430) the diagnostic criteria for the sprue syndrome and gives the case histories of four patients who exhibited refractivity to the form of treatment which in the great majority of patients suffering from sprue yields prompt and brilliant results. In such cases the morbid process appears to be irreversible. The reason for this occasional refractivity is not known

The sprue syndrome of the adults and the caeliac disease in the children are identical pathological disturbances and both respond very satisfactorily to parenteral liver extract with Vitamin B complex added to it, together with low fat, high protein and high vitamin diet, "Liver-banana-vitamin" therapy

The diagnostic requirements of the syndrome are

- 1 *Steatorrhoea*—average fat in the dried stools 48.5%, Normal 15% or less
- 2 *Loss of Weight*—as marked constant feature, from 25 to 75 lbs or as much as the present weight of the patient on examination
- 3 *Low Glucose Tolerance Curve*—A rise of less than 40 mgm per 100 cc of blood, in the blood sugar curve when given 1 gm of glucose per kilo of body weight
- 4 *Anaemia*—Macrocytic hyperchromic anaemia
- 5 *Hypochlorhydria* or *achlorhydria* after histamine stimulation in untreated cases. After treatment the acidity returns to normal in about 80 per cent of the cases. In only about 20% there is achlorhydria after histamine injection

Other features—sore, depilated, reddened tongue, with or without aphthous ulcers, pendulous, gaseous abdomen, distended colon borborygmi, etc., fill in the clinical picture but are not necessary for the diagnosis. Of the above five criteria, *Steatorrhoea* is the most important and a quantitative estimation of the fats in the stools may often be necessary to establish the diagnosis of sprue. The differential possibilities to be considered are 1 pernicious anaemia, 2 multi-

ple avitaminoses 3 pancreatic disease, 4 tabes mesenterica, 5 gastro-colic fistula, 6 Anorexia nervosa, 7 Simmond's cachexia

Recent observations reviewed by Doyné (The Practitioner, Nov 1942, p 309) suggest that the sprue syndrome results from damage to the villi of the small intestine. Phosphorylation of fats takes place on the epithelial surface of the villi. Damage to the villi lessens or prevents the absorption of fats, and may also lead to the non-absorption of vitamins, which is more important than the absence of the latter from the diet of these patients.

Manson-Bahr (1941) advocates the administration of nicotinic acid and of riboflavin in the treatment of sprue, besides the use of large doses of liver extract and a suitable diet. Nicotinic acid in doses of 150 to 300 mgm daily alleviates the mouth symptoms, and riboflavin in 3 mgm doses daily relieves the angular stomatitis. L I I

THE PATHOGENESIS OF THE SPRUE-SYNDROME

A Hurst (Guy's Hosp Reports, Vol 98, p 1-21, 1942) believes that tropical sprue, non-tropical sprue (or 'idopathic streatorrhoea', and coeliac disease or "Herter-Gee disease") are varieties of the same disorder—the "sprue syndrome" which differ only in the part of the small intestine in which they originate and the age of the patient. There are certain characteristic and constant features of the sprue syndrome:

(1) the stools contain excess of split fat in the form of fatty acid and soap crystals, but no excess of neutral fat, meat fibres or starch, and no inflammatory material,

(2) radiography demonstrates the disappearance of the normal feathery or herring-bone pattern of the duodenal and jejunal mucous membrane produced by the valvulae conniventes (Snell & Camp, 1934, Kantor 1939, Golden, 1941)

(3) no pathological changes are found in the intestine after death if post-mortem changes are prevented (Thaysen, 1932 Mackie & Fairley 1934)

With adequate treatment normal absorption of fat is restored together with the normal radiographic appearance of the duodenum and jejunum.

The author suggests that the characteristic features of the sprue syndrome are the result of paralysis of the *muscularis mucosae*. This would lead to loss of the pumping action of the villi by means of which fat is conveyed from the lacteal radicles of the villi into the larger lacteals, and to flattening of the valvulae conniventes, the constantly changing pattern of which depends upon the activity of the *muscularis mucosae*, without any accompanying pathological changes in the mucous membrane. Paralysis of the *muscularis mucosae* may be secondary to loss of the normal stimulants of Meissner's plexus, from which it derives its nerve supply, or to the effect of vitamin deficiency or some toxæmia on the plexus.

An exception must be made for those cases of the sprue syndrome associated with disease of the mesenteric glands in which the hindrance to fat absorption occurs at the level of the glands instead, of in the villi.

Book Reviews and Notices

REPORT ON THE ECONOMIC AND NUTRITION SURVEY OF GUJARATI MIDDLE CLASS FAMILIES IN BOMBAY CITY January 1943 issue of The Journal of the Gujarat Research Society By Dr V V Shah, M.D and Dr M H Patel The Gujarat Research Society, Bombay, pp 72, price Re 1/

To avoid any misunderstanding we would suggest that the words "Hindu, strictly vegetarian," should appear before the Gujarati Middle Class Families, because the investigation was confined to this class only. Looking to the number of statistical tables and the detailed economic and nutritional related information, our first impression was that this was a respectable solid work, so very necessary in arriving at right conclusions in such surveys. But we are constrained to say that when we put the volume down after reading it through, we were left with a feeling that our expectations have not been fully realised. Looking to the enthusiasm displayed and the trouble taken, it is all the more a pity that the survey is not as complete as it should have been so that some reliable solid conclusions may be drawn and appropriate recommendations may be made with some confidence.

While it was originally contemplated to investigate the histories of at least 1,000 families for economic and nutritional status, unexpected difficulties cropped up owing to the exodus due to the war scare and these were further increased by rising prices and difficulty of getting foodstuffs even to satisfy the ordinary wants, leave alone the question of quality. And the inquiry had to be closed down after data had been collected, on the economic side for 380 families and on the medical side for 193 families only. Even this calamity would have saved the inherent quality of the investigation if it could have been sufficiently extensive. But, unfortunately that was not the case. The entire work of investigation was carried out by two post-graduate workers, Dr V V Shah on the nutritional side and Dr M H Patel on the economic side, with the help of a lady health visitor. While the major part of the work consisted of taking down information obtained in response to a questionnaire, (no actual experimental prescribed diet control and its effect on nutrition in a given number of volunteers or experimental animals being part of the nature of this inquiry), the only and really valuable part of the nutritional inquiry, viz, the nature and quantity of foodstuffs, etc., taken by various members of families investigated was gone into *only once*, as is made clear by one of the joint authors in the following words, on page 30, "This type of family survey—dietary survey by family method—was conducted for one day only and that too by a single visit of the lady health visitor," and it was not found prac-

"The quantitative as well as qualitative deficiency in spite of adequate provision of funds in several cases can be explained by waste, the lack of skill in management, and gross ignorance of the elements of nutritional science"

Regarding the Schedule of Balanced Diet on page 72, for a middle-aged person doing normal work (by the way what is *normal* work? We presume the author means by it, sedentary, not hard, work as is the case with lower middle class Gujarati clerical workers and business employees) we would like to say that it is good of its kind as an ideal to be aimed at but hardly likely to be achieved. We would very strongly suggest that in further continuation of this survey more attention may be paid to the absolute minimum food-stuffs necessary for optimal health, bearing in mind all the time the inadequacy of income of the people concerned, so that it could be given a practical effect in everyday life as we find it. That should be the only real aim of any dietetic survey or investigation.

The Gujarat Research Society has been able to carry out this survey through the munificence of Sir Purshottamdas Thakurdas who bore "the cost not only of the Economic and Nutrition Survey, but also the cost of printing the Report of the Survey!" For this generosity the Gujarati Community should thank the millionaire knight and should rejoice that rich merchants are taking interest in scientific investigations. But alas, the modern scientific investigations cannot be carried out adequately by individual small donations, however well meaning. What is needed is a well endowed research institute for studying nutrition in man and animals, fully equipped with trained full-time workers and with up-to-date laboratory for experimental work. Surely there are sufficient millionaires in Gujarat who can endow not one but half a dozen such institutes, if it is possible to rouse their social conscience. Failing this, perhaps the best way to get the work done is through the State. The Gujarat Research Society should exert its influence on the government to institute work on these lines for different communities of Gujarat. Special inquiries are also needed for industrial workers as well as for workers on the farms. We hope the Gujarat Research Society will continue the good work it has started, with the help of Sir Purshottamdas, and the adverse conditions due to war will not damp its enthusiasm.

S K V

BLOOD TRANSFUSION by K N Jejurikar, LCPS (Bom). A pamphlet of 14 pages published by the author at 1349, Shivajinagar, Poona 5. Price Re 1/- We do not know for whom this pamphlet is meant. The information contained in it is most elementary and there is nothing to show the writer's special experience or ability to commend it to medical men. It is full of printer's errors and we do not like the idea of diverse advertisements in a medical pamphlet.

News & Notes

TRANSMISSION OF EQUINE ENCEPHALITIS TO MAN

Dr R Cibils Aguirre, a pediatrician and director of public aid of Buenos Aires, recently directed attention to the transmission of equine encephalitis to man. Dr Valdez of Cordoba and his collaborators reported several cases of encephalitis in children which were coincident with an epidemic of encephalitis in horses. They have seen 36 cases, and Hanon and Boidecl have seen about 20 cases.

ELECTROENCEPHALOGRAPHY

A new laboratory of electroencephalography has been opened at Sanford University School of Medicine, San Francisco. The new instrument has been under construction and adjustment for nearly ten months. At present the new laboratory is being used part of each day for testing by the military services. The electroencephalograph just completed is unique among such apparatus in that it is entirely remotely controlled, thus avoiding electrical interference. It holds a newly invented automatic calibrating device to give instant interpretation of the currents being recorded.

INDIAN MADE LIVER EXTRACTS

At present there is a great dearth of foreign made liver extracts and one would like to welcome the enterprise of Indian manufacturers to produce potent liver extracts for clinical use. Dr Das Gupta of the School of Tropical Medicine, has tested the therapeutic efficacy of some of these preparations and arrives at the conclusion that "In the treatment of tropical macrocytic anaemia the results are never as uniform as in the treatment of pernicious anaemia. Accurate appraisal of the efficacy of any drug is therefore, not possible. The results obtained with T C F WHOLE LIVER EXTRACT are in the same category as those obtained with the best crude liver extracts of foreign manufacture, the results obtained with CIPALON are also quite good. The results obtained with the purified extract (T C F Plain) are definitely of a lower order, but the result obtained with this purified liver extract on a case of pernicious anaemia was highly satisfactory" (Ind Med Gaz, Jan 1943, p 34-37).

MEDICAL CONGRESS ON RECENT ADVANCES IN MEDICINE

A medical congress of the independent medical profession and members of the army medical service is to be held in the Anatomy Lecture Theatre of the Grant Medical College, Bombay, on the 12th June, 1943, at 2-00 p.m. (S.T.) Short papers of 20 minutes duration followed by 10 minute discussion will be read on Recent Advances in Medicine and Surgery. Members of the medical profession and senior students from medical colleges and schools are cordially invited to attend.

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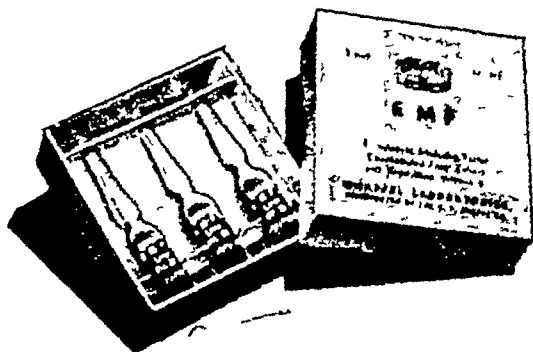
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Original Contributions

ANGINA PECTORIS IN PAST AND PRESENT WITH SPECIAL REFERENCE TO ITS MODERN TREATMENT

By
ROBERT HEILIG,

M D

First Physician, Krishnarajendra Hospital & Professor of Medical College, University of Mysore

No more stimulating experience could be imagined than that which rewards a historically minded physician for studying the original writings of medical pioneers, thus tracing the humble path or the sky-high flight which led to immortal discoveries. Having at their disposal not one of the clinical methods without which to-day none of us would dare to approach his patients, they worked out the main syndromes, which form the backbone of our present clinical system, with astounding precision. One of the most impressive examples of this kind is William Heberden's classical description of the condition which he called *angina pectoris* (1772). He was not the very first to observe it. Good accounts of this disease are to be found in the Earl of Clarendon's memoirs (case of Henry Hyde, 1632), in Morgagni's epoch making work on "The Seats and Causes of Diseases investigated by Anatomy" (1761) which contains the sum total of the life work of this giant who laid the foundations of anatomical and clinical pathology, his case report of *angina pectoris* dates back to 1707, his post mortem findings of coronary sclerosis to 1743, just 200 years ago. And, yet, Heberden's merits are undisputed because of the masterly way he summarized in a short paper almost everything of what we know about the various features of this complex syndrome, its age-

* See the interesting collection "Cardiac Classics", ed. by Williams & Keys (1941)

and sex-incidence, its changing from short spasmodic attacks, starting on exertion, especially after meals, with all the typical and a good deal of atypical irradiations, to the long lasting pain in inveterated cases of which we know now that it is due to an extreme coronary stenosis which does not permit any dilation or to an occlusion of the coronary artery. He points out the absence of dyspnoea, the possibility that the attack could be "brought on . . . even by swallowing, coughing, going to stool, or speaking, or any disturbance of mind." He has "seen nearly a hundred people under this disorder" prior to formulating the historical definition in which the name was used for the first time, he says "the seat of it, and sense of strangling, and anxiety with which it is attended, may make it not improperly be called angina pectoris." Even the nature of the pain was clearly recognized by him "it belongs to the class of spasmodic, not of inflammatory complaints." The prognosis was worked out and illustrated by several of his observations. Little he has to say about the therapy "Quiet, and warmth, and spirituous liquors help to dispel the effects of a fit when it does not soon go off. Opium taken at bed-time will prevent the attacks at night." Less understandable is his remark that he knows "one who was nearly cured by sawing wood for half an hour every day", should this have been a case of neurosis or one of obesity, suffering from some chest pain due to the diaphragm being raised by flatulence?—Fascinating reading makes also the account of *John Hunter's* angina pectoris attacks, prefixed to his posthumously published "Treatise on the Blood Inflammation and Gun-shot-wounds" by his brother-in-law *Everard Home* (1794) who was eye-witness of "the agonies he suffered" and who handed down to posterity how the greatest physicians of this time failed in giving any relief to their illustrious patient. To him Hunter confided his observations on himself as well as his request that a post mortem of his heart should be performed. The pathological report contains the significant statement "the coronary arteries had their branches in the state of bony tubes, which were with difficulty divided by the knife," findings which show a striking analogy to those recorded in another classical post-mortem, performed on Sir James Mackenzie's heart by *J Parkinson* (1925), published by *Waterston et al* (1939). It is an amazing fact that so many pioneers in medical sciences died of angina pectoris, *John Hunter*

(1728-1793) whom W. Boyd calls the thunderbolt of surgery, L. Traube (1818-1876), the undefatigable fighter for experimental medicine, H. Nothnagel (1841-1905) whose pioneer work on intestinal obstruction and angina pectoris, together with his noble personality made him the personification of an accomplished physician in pre-war Imperial Vienna, Murrell (1853-1912) who introduced nitro-glycerine in the treatment of angina pectoris, Sir James Mackenzie (1853-1925), on whose life-work modern cardiology was built and many others. This sad list of famous names induced my great teacher K. F. Wenckebach (1864-1940), who was the first to recognize the true nature of extrasystoles in man, to retire from his professorship at the age of sixty, ten years prior to the compulsory age limit, being convinced that every overworked medical man is threatened by this scourge, being, as it were, a potential victim of it. This experience of the all-importance of psychic factors in the aetiology of the anginal attack found a picturesque expression in the words of John Hunter that his "life was in the hands of every rascal who chose to annoy and to tease" him.

Prior to turning from those who, by keen observation of others or themselves, first recognized the characteristic clinical features of angina pectoris to the ways and means of alleviating the suffering which is caused by it, it is necessary to differentiate between two conditions which mainly are responsible for the syndrome of deep anxiety, mostly accompanied by some pain of varying intensity, of characteristic localization and peculiar irradiation which is called angina pectoris. These conditions are coronary stenosis and coronary occlusion, the latter is practically always due to an arterial thrombosis. In both these conditions a discrepancy between the amount of blood required by the heart muscle and the amount actually supplied through the coronary arteries is the cause of the complaints. In coronary stenosis this disproportion becomes manifest usually when an increased supply is required on exertion or excitement, after a large meal, etc., or if upon the chronic stenosis an acute spasm is superimposed which still further cuts down the blood-supply, such as may happen under the influence of low temperature. Thus, in coronary stenosis the heart muscle receives just the amount of blood necessary for preventing muscular ischaemia if none of the factors are in operation which either increase the circulatory requirement or diminish the available blood volume. Anatomically, two quite different processes might cause a coro-

nary stenosis and lead to the same functional result of myocardial ischaemia which causes the anginal pain. One is an atherosclerotic involvement of the coronary arteries, transforming the vessel into the stiff, sometimes widened, sometimes narrowed tortuous tube with thickening of the walls which already is described in the post-mortem report of Hunter's heart (*loc cit*) and with many details and measurements in that of Mackenzie (*loc cit*). It is obvious that such a vessel is unfit to supply quickly varying blood volumes according to varying requirements. A further danger point in this condition is the development of a thrombus on the roughened atheromatous inner surface of the coronaries. However, the outlook for maintaining some degree of viability for several (5-10) years is much better in a stenosis due to coronary sclerosis than in one caused by "coronary" syphilis, the other ordinary cause of angina on effort. Here, the vessel walls are entirely free from pathological changes and, yet, a syphilitic stenosis is an extremely treacherous disease. This is easily understood by the anatomical facts which reveal that in syphilitic mesaortitis the coronary ostia are extremely narrowed by the syphilitic infiltration and proliferation of the aortic walls. Not rarely it is impossible to introduce the thinnest probe into the coronary lumen so that the slightest change in the wrinkled, tree-bark-like looking aortic walls suddenly may completely occlude one coronary ostium, if also the other one is badly stenosed sudden death is the consequence. Other conditions, occasionally leading to anginal attacks, in spite of normal coronary arteries either are characterized by a deficient blood-and oxygen-supply to the myocardium, such as low atmospheric pressure, severe anaemias or aortic regurgitation, or by an increased blood-oxygen-requirement, such as hyperthyroidism or, finally, by a combination of both these factors which are operative in paroxysmal tachycardia. Absolute or relative inadequacy of blood-supply causes myocardial ischaemia and, thus, anoxia with a subsequent accumulation of abnormal metabolic products, the subjective expression of this disturbance of muscle chemistry is pain which is of the same origin in intermittent claudication as well as in angina pectoris (*Lewis, 1936*)

In coronary thrombosis the blood supply is suddenly cut off from this area of the myocardium which is dependent upon

the occluded coronary branch, the coronary arteries being functional (not anatomical) end-arteries, a varying length of time is required to activate a collateral circulation. These differences in the underlying mechanism together with the anatomical changes following a coronary occlusion make it understandable that the clinical manifestations of coronary stenosis and thrombosis widely differ, though both have the subjective sensation of angina pectoris, caused by the insufficiently perfused myocardium, in common. Their differentiation is of great importance because each of these conditions requires and, especially, forbids certain therapeutic measures peculiar to it, though some are useful in both of them. One cannot overestimate the merit of those physicians who worked out the clinical diagnosis of coronary thrombosis, thus enabling us to avoid mistakes in prognosis and therapy. Their achievement is still more praiseworthy as they succeeded in their attempts either long before the electrocardiograph was invented or used for clinical purposes.

The first to make the correct diagnosis of coronary thrombosis in vivo was *Hammer* (1878) in Vienna, the clinical symptomatology was adequately described by *Obrastzow* and *Straschesko* (1910). The classical report, drawing such a vivid picture that everybody who sees such a case must recognize it at once, was published by *Herrick* (1912), based on seven cases with two autopsies. He emphasized on anatomical and clinical grounds, that a coronary occlusion might survive for some time and that even a functional recovery should be possible, though none of *Herrick's* cases lived longer than one week after the thrombosis had developed. Peculiarities of this serious condition such as the resemblance to surgical abdominal conditions, the ensuing pericarditis, the contrast between extreme weakness and perfect clearness of mind are masterly featured. And yet, one is amazed to see this great clinician recommending strophanthine and digitalis as the routine treatment, arguing against those who are afraid of the latter drug "in cases in which the myocardium is weak."

The main differences between angina pectoris due to coronary stenosis, which owing to its frequent onset during exertion is called angina on effort, and that, occurring in coronary thrombosis could be tabulated in the following way

TABLE

Signs and Symptoms	Coronary stenosis	Coronary thrombosis
onset of pain	during or immediately after exertion, excitement or exposure to cold	without provocation or long afterwards, during rest or sleep
duration of pain	up to 30 minutes	lasting for hours
localization	usually typical	frequently atypical
pulse	full rate hardly altered	feeble rate increasing
blood pressure	not altered or increased	falling pulse pressure reduced
effect of nitrates	prompt relief	no effect
appearance of patient	varying pale or flushed	pale, tending to livid discoloration covered with perspiration
behaviour of patient	avoids any movement	restless up to rolling about
AFTER-EFFECTS		
temperature	normal	fever from 2nd day onwards
leucocyte count	normal	increased 10,000-20,000 per c mm
sedimentation rate	normal	increased
urine	not altered	frequently glycosuria
pericarditis	absent	not rare after 2nd day

The table shows that, apart from the anginal pain these two conditions have got hardly anything in common. It should be possible, at least in typical cases, to distinguish between them on clinical grounds, even if an electrocardiogram is not available. Especially the signs, called in the table "after-effects" definitely prove the presence of a thrombus, all of them, except for the glycosuria, being due to the myocardial infarction. Fever, leucocytosis, increased sedimentation rate and pericarditis episternocardica are caused by the necrotic muscle area and its absorption.

With the help of an electrocardiogram there is rarely any difficulty in establishing an early diagnosis beyond doubt. In coronary stenosis the electrocardiogram of the resting patient either is within normal limits or shows signs of a myocardial lesion such as a depressed S-T or a low T. In many cases after an exertion test (climbing of steps or knee bending) a previously normal electrocardiogram presents the features just mentioned, whereas a pathological one shows an increased depression, a still lower or even an inverted T. In coronary thrombosis the pathognomonic changes (*Pardee*, 1920) appear predominantly in lead I if the thrombus occludes a coronary branch on the anterior ventricle wall (mostly left coronary artery), in lead III if the posterior wall is affected. It is important to know that sometimes no electrocardiographic changes are apparent within the first 12 or even 24 hours following the onset of the attack, but on the second day the "high take off" and (frequently) a deep Q in lead I or III, and the accompanying characteristic changes in

lead II and IV dispel any doubt, the development of the spike shaped "coronary T" in the same lead where initially the "high take off" appeared develops about one week later and marks the beginning of a slowly progressing repair. It seems desirable that the practitioner should know something about these possibilities and limitations of electrocardiography to make the proper use of this extremely helpful branch of cardiology.

The differential diagnosis between stenosis and thrombosis had to be treated at some length with a view to facilitating a decision upon the treatment, most suitable to each of these two conditions. It is generally known that *nitrites* cut short an attack of angina on effort, arising from coronary stenosis. Sir Thomas Lauder Brunton (1867) introduced "nitrite of amyl" in the treatment of anginal attacks, it is still used in doses of 2-5 minims by inhalation from crushed glass pearls or capillaries, although its effect starts almost immediately, i.e., in 10-15 seconds, it has got disadvantages which restrict its usefulness. Its effect frequently lasts shorter (7 minutes) than the attack so that after some relief was obtained the pain starts again. Among all the nitrites it has the maximum diminishing action upon the blood pressure which in cases with a low pressure or a badly damaged myocardium is not desirable, finally, the unpleasant smell and the high price are prohibitive in many cases. Very much better is the effect of nitro-glycerine (Glycerylis Trinitratis B.P.) which starts after one minute and lasts for one half up to one hour. Introduced by Murrel (1879), it is one of the most reliable drugs in the treatment of an anginal attack, the usual doses are 1/200, 1/100 up to 1/50 grain. It is essential to instruct the patient that the best method of using it is by the perlingual route. If tablets are used, they should be crushed and kept under the tongue. But tablets are not quite reliable in our experience, nitro-glycerine losing its effect by storage in this form, we prefer the prescription of a 2 per cent alcoholic solution, one to two drops of which are applied on the dorsum of the patient's hand and licked without swallowing it, this secures the perlingual administration in an effective form, the single dose of 2 drops being about 1/50 gr. Sodium nitrite ($\frac{1}{2}$ to 1 grain) acts after 15 minutes for about 2 hours, therefore, it is useful only for preventive treatment for which purpose erythrol tetranitrate is by far superior. In doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain it protects the patient against an expected attack, becoming effective after 30 minutes and acting for 5 hours. Thus, such a dose should be

taken about half an hour before rushing to a train or prior to being exposed to some probable cause of excitement, such as business or political meetings, delivering of a speech, seeing a lawyer on controversial matters and, especially, sexual intercourse which involves both the dangerous factors, bodily exertion and mental excitement. Another group of preventive drugs are the purine—or xanthine—derivatives whose effect is enhanced by combining them with sedatives, such as bromides or barbiturates, and specific coronary dilators such as erythrol tetranitrate which in such a combination is effective in very small doses. We prescribe theobromine pur $1\frac{1}{2}$ gr (0.1 gm) or theobromin sodium salicylate, 5 gr (0.3 gm) with phenobarbital $\frac{1}{12}$ to $\frac{1}{6}$ gr (0.005–0.01 gm) and erythrol tetranitrate $\frac{1}{20}$ to $\frac{1}{10}$ gr (0.003–0.006 gm) in capsules to be taken thrice a day. Ready made preparations, containing theobrom sod salic and luminal are available as Theogardenal "M & B", Theobital "Cipla", Theominal "Bayer", etc. The most valuable member of this group is theophylline ethylenediamine (Aminophylline "B. W. & Co", Cardophyllin "Wheniff", Theamine "Lilly", Minaphil, Euphyllin "Byk", Deriphyllin "Homburg", etc). According to clinical (Marvin, '26, Musser, '28, Smith, '28) and experimental (Gilbert et al, '29, Fowler et al, '35, Gold et al, '37) facts there cannot be any doubt that this compound is a powerful dilator of the coronary arteries, the effect of which lasts for many hours. It is a curious fact that the most recent British text books (Lewis, 1942, Dunlop et al, 1943) mention only the oral administration of theophylline ethylene-diamine which not only is almost ineffective but also irritates the stomach. In India where the use of suppositories meets with various difficulties, only by intramuscular or, still better, by intravenous administration the advantages of this drug could be fully utilized. With the present dosage of 4 grains (0.24 gm) per ampoule (2 c.c. for the intramuscular, 10 c.c. for the intravenous route contain the same amount of the substance) not the slightest by-effect is noticed, sensations of nausea, hyperpnoea etc, frequently observed when the original brand Euphyllin was used, have been due to the high concentration of the solution which contained 8 grains per ampoule. Having used theophylline ethylenediamine for the last 24 years in the treatment of angina pectoris, we are sure that it is the most valuable drug for improving the myocardial blood-supply in coronary stenosis as well as in coronary thrombosis, forming the common link

in the medication of these different conditions After ten to fifteen injections of any brand of this compound, administered by the intravenous or intramuscular route, on consecutive days in the beginning, in slightly longer intervals towards the end of the course, the efficiency of the heart muscle in coronary stenosis considerably increases due to dilation of the coronaries, thus, an amount of exertion which regularly excited the pain of myocardial ischaemia, prior to this medication, could be borne afterwards without any discomfort With the effect of theophylline ethylenediamine in coronary occlusion we have to deal later on Another group of remedies, the value of which is much doubted in authoritative text-books, are the muscle extracts, frequently, though wrongly, called heart hormones The essential substance in these extracts is adenylyl-pyrophosphoric acid which plays an important part in the physiology of muscle contraction There is a great difference in the effect of the various makes One of the best known among them, frequently used in this country, was Lacarnol "Bayer" of which we never saw any convincing results, but there have been others such as Myoston "Henning" or Embran "Saxon Serum Works" by which sufferers from angina on effort were definitely benefitted The only preparation of this kind, here available at present, is Corhormon "Cipla" which in some cases affords a certain amount of relief and achieves even some improvement of the myocardial condition as seen in serial electrocardiograms Less divided is the opinion about the usefulness of sex hormones in properly selected cases One of the most distressing complaints in females approaching menopause or being in the climacteric phase is a feeling of oppression in the chest, increasing up to a choking sensation, palpitations, which always are absent in coronary stenosis, sometimes even some pain or numbness irradiating towards the left arm, anxiety, perspiration and other vasomotor disturbances The difficulty in making the diagnosis of a climacteric condition and excluding a real coronary defect lies in two objective findings, characteristic for such cases, a blood pressure which usually is moderately increased and an electrocardiogram which shows a depression of S-T especially S-T₂, and a low or even inverted T Only by knowing these facts and drawing the necessary inference regarding the right way of treatment, these patients could be saved years of serious discomfort and unnecessary limitations of activity,

apart from the depressing feeling of being invalids which just at this period of life may lead to grave mental consequences. The use of oestrogens (Ovocyclin, Theelin, Menformon, Dimenfoimon or the synthetic hormones Stilboestrol, Clinoestrol, etc) improves the condition to a surprising extent. Usually it is sufficient to give one tablet of 1 mg per day of the "natural" hormone (oestradiol) and one injection of its propionate or benzoate ester (1 mg per dose) twice a week. Stilboestrol, administered in tablets of 5 mg each once a day, should have a similar effect. Quite recently good results of testosterone injections have been reported in angina on effort in men. A very promising method of treatment was introduced by Raab (1941). He found that patients, suffering from angina on effort show a larger amount of adrenocortical compounds in the circulation, especially after exertion, than normal ones. Therapeutic X-ray irradiation of the suprarenal glands diminishes the amount of these pressor substances and abolishes the anginal attacks in the majority of such patients. The latest addition to our therapeutic armament is the use of nicotinic acid or niacine (Neuwahl, 1942) in coronary stenosis which, administered by intravenous injection or even dripping infusion, is reported to give excellent results. One of the older drugs which is appreciated, especially, by stout, "plethoric" patients with a tendency to an increased blood pressure is potassium iodide instead of which compounds of more recent origin, such as Iodalbin or injectable iodine preparations, such as neutral iodine, Entodon or (the India made) Yodopil could be administered. In properly managed cases it should not be necessary to use morphine or its derivatives, the danger of habit formation being extremely great in such a chronically recurring painful condition. Morphine-free analgesics and spasmolytics will be treated when we deal with coronary thrombosis. The use of whisky, apart from opium, the only remedy which Heberden found useful in alleviating the pain, is still advocated in British text-books. A few words have to be added on local treatment of the pain sensation. One useful method of this kind consists in counter-irritation. A highly effective means to achieving this purpose is bee-venom (Apicur "Roche"). The present writer found this remedy useful in such cases where, when the attack had subsided some pain remained in the precordial region, the shoulder, interscapular region or in the area of pain irradiation along the nerve plexuses, a condition which, apart from the lasting discomfort, constantly reminds the patient

of the threatening next paroxysm. One localizes carefully with the help of the patient the maximum of the persisting pain and produces in and around this spot an increasing amount of weals by injecting 0.1 c.c. of bee-venom intradermally, from two weals at the first administration up to ten at the last, occasionally a short lasting exacerbation of the anginal pain occurs. Distilled water and plenocaine are decidedly inferior to bee-venom, a course of which frequently secures a considerable relief for many weeks. Another way of alleviation by local treatment consists in producing squares of erythema at the maximum localization of the anginal pain by irradiation with ultraviolet rays, a method which sometimes gives very good results, superior even to those achieved by x-ray therapy. Useless is diathermy treatment, unreliable, because rarely helpful, short-wave administration. It is not within the scope of this paper to deal with semi-surgical and surgical attempts of preventing anginal attacks. Paravertebral alcohol injections around the left upper five thoracic ganglia, ganglectomy of the left stellate ganglion, resection of the depressor nerve should interrupt the reflex arc. Subtotal thyroidectomy, which occasionally yields surprising results, acts by diminishing the blood requirement of the myocardium.

Of equal importance as the use of the right kind of remedies or physio-therapy is the management of the patient's everyday life. First of all, the occasions, which, according to the patient's own experience, bring on his attacks have to be covered with nitrites taken in advance or, if possible, by an aminophylline injection. Many of them such as hurry, excitement, working "under pressure" could be avoided if the general rule of "take it easy" would be applied religiously, but, unfortunately, many of these patients are quick tempered, high-strung, over-ambitious professional or businessmen who feel their responsibility more than others and suffer from these features of their psychic constitution which are shortcomings from the medical viewpoint, although they made them a success in life. Of the greatest importance is the somatic constitution of such cases. If they are tending to overweight, mostly due to over-eating, to hypertension and diabetes, weight reduction by food restriction sometimes gives almost immediate relief, thyroid medication has to be avoided, anginal pain being provoked by it. Nicotine abstinence and alcohol temperance are essential, there is no other pathological condition, except for peptic ulcer, where it is equally

imperative to insist upon entirely giving up smoking Sexual intercourse should be limited to the minimum requirements of the individual case Interest in quiet hobbies such as philosophy, history or stamp collecting are of great help in relaxing, one of the few things these patients are slow in doing If a change of environment seems desirable, an altitude over 4,500 feet above sea level should be avoided, the selected place should be free from mist, protected against cold winds and should afford possibilities for walks on level ground, hill climbing or walking against the wind being some of the factors which regularly cause anginal attacks

All these ways of treatment and general management are indicated in atherosclerotic as well as in syphilitic coronary stenosis It remains to discuss the scope of specific medication in the latter condition, the diagnosis of which rests upon a positive W-R and the radiological signs of a mesaortitis The age incidence no more is a differential feature since coronary sclerosis recently becomes manifest in the fourth decade with increasing frequency There is no difference of opinion about the necessity and advantage of iodine administration in "coronary" as in every other vascular syphilis, full doses of potassium iodide should be given, 30 grains t.i.d. and even more if no signs of iodism appear Bismuth should be injected simultaneously or alternating with courses of iodide But it is an open question whether organic arsenicals are indicated or whether they should be avoided It seems to be certain that every effective arsenic treatment, irrespective of the selected drug, whether it be Neo-salvarsan, Mapharside, Novarsan or any other compound of this kind, might cause focal reactions (Jarisch-Herxheimer) in the syphilitic lesions, if such a reaction, which is accompanied by hyperaemia, takes place in the aortic wall near the coronary ostia, it may lead to their occlusion with all the dreaded consequences Therefore, if any one of the organic arsenical compounds should be employed at all, it should be used in one-tenth of the usual dosage, taking Neo-salvarsan as an example, the first dose should be 0.015 gm, the next 0.03 gm and so on and the maximum single dose should not exceed 0.09 or 0.15 at the utmost As a matter of course, patients under this treatment have to be carefully watched and at the first sign of an increased intensity, frequency or duration of pain the administration should be stopped at once

Coronary thrombosis is one of the few conditions in internal medicine where the fate of the patient to a considerable degree depends upon the experience of the physician-in-charge of the case. The "don'ts" are of such a paramount importance in saving the patient's life that it may be permitted to start with enumerating them, prior to giving positive advice. Nitrites are not only useless in this condition but contra-indicated because they cause a further reduction of the already falling blood pressure. Adrenaline, ephedrine and similar preparations are extremely dangerous owing to the fact that—contrary to theoretical expectation—in many cases they cause a spastic constriction of the coronaries which might prove fatal. Coramine, cardiazol etc should be withheld, even if the pulse is very feeble, unless the systolic blood pressure falls below 75 mm Hg, the level below which circulation cannot be maintained, one has to keep in mind that these drugs have no fortifying action upon the heart, they act by increasing the vessel tone and, thus, increase the burden upon the heart muscle. Equally or even more strictly contra-indicated is the use of digitalis, at least during the first eight to ten days following the attack, though not all cardiologists are agreed upon this point, it seems very risky to enforce more powerful heart contractions when utmost care has to be taken to limit the wear and tear to the unavoidable minimum. Moreover, in such a badly damaged myocardium digitalis and strophantine frequently release ventricular extrasystoles which in these circumstances not rarely lead to fatal ventricular fibrillation. Another warning has to be directed against the early use of organic mercurial diuretics, introduced into therapy under the joint authorship of the present writer (*Saxl & Heilig*, 1920), they proved of the utmost benefit in every kind of heart failure, even when no oedema was visible (left heart failure with pulmonary congestion), except for two conditions where their administration is definitely dangerous, viz, in the failing heart of any stage of glomerulonephritis and within about a fortnight following coronary thrombosis. In the latter condition the danger lies in the fact (*Saxl & Heilig*, 1922) that following the injection of such a diuretic, the fluid which was deposited in the subcutaneous tissue and in the liver is forced back into the circulation prior to its being eliminated through the kidneys. During these successive phases of water and salt, passing through the circulation, the burden laid upon the heart is increased, the heart has to work against a higher resistance in the periphery and not so

rarely, within 12 to 24 hours after the mercury administration, it breaks down owing to the extreme myocardial weakness. The last of these negative advices is concerned with our attitude towards the patient. "Don't compromise" is the supreme rule. As soon as shock and pain are over a good many of these men, used to be obeyed as bankers, lawyers, planters, industrialists etc., most of the victims of coronary thrombosis in this country belonging to these upper classes, demand more or less categorically some facilities for attending to their affairs. Whenever such a situation arises, absolute, even brutal frankness is unavoidable, it is one of the few occasions in medical practice where hiding the truth from the patient might prove fatal to him. While explaining the danger points we do not emphasize so much the possibility of a sudden death, if the patient fails to keep almost motionless for three weeks, as the certainty of weakening the heart muscle for good by not giving it a chance to form a firm scar in the "punctured" area. In this condition the patient's unconditional co-operation is so essential that, but for it, a satisfactory management is hardly possible, every effort from the physician's part should be made to secure it. An instructive illustration of the social incidence of myocardial infarction is furnished by the distribution of these cases among general and special wards in Mysore. In the former, comprising 92 medical beds, fully occupied throughout the year, about one case of this kind is seen every two years, being found in male Brahmins, previously suffering from essential hypertension or diabetes. The special wards consist of 21 beds, medical as well as surgical, used as need arises, in the average of the year about eight of them are required for medical cases. And yet, there is hardly one week when not one of those beds was occupied by a fully developed coronary thrombosis. Analysing the communal distribution we find about one-half of them being Europeans, here usually planters, from 50 to 75 years old, most of the other half belong to the Brahmin community, they are officials, retired from responsible positions, 56 to 65 years of age. Within the last three years we have seen a coronary thrombosis only once in a Mohamedan, a retired school headmaster, vigorously working as a politician.

The medical treatment of coronary occlusion is comparatively simple. In the beginning, pain and, especially, restlessness have to be combated. Morphine in sufficient doses is strictly indicated, we start with $\frac{1}{3}$ grain of morphine with $\frac{1}{200}$ grain atropine,

followed after one hour by $1/4$ grain of morphine plus $1/200$ atropine if the pain has not subsided or if the patient is still restless. During the following two days we prescribe morphine-free analgesics, among which Cibalgin, Spasmo-Cibalgin or Spasmin-don in doses of 1-2 tablets four to five times a day proved very useful in saving further morphine administration, apart from the analgesic action they exert a considerable sedative effect. From the second day on, every day for about three weeks one aminophylline^{*} injection (0.24 gm) is given, preferably by the intravenous route, we have never seen any untoward by-effect, in the long run the intramuscular administration, probably, has the same effect, the moderate local pain, caused by it, could be avoided by infiltrating the gluteus with plenocaine (1-2 cc of a 2 per cent solution). The early commencement of aminophylline medication is of decisive importance because it is the only means of enforcing the opening of a collateral circulation on which the repair of the myocardial lesion depends. The rest of the medical treatment in uncomplicated cases consists in preventing bronchitis and flatulence. For the first purpose Resyl "Ciba" injections, for the second charcoal preparations combined with mild laxatives (Carbindon etc.) could be used. A sufficient amount of sleep should be secured to which end paraldehyde in one dram doses is the drug of choice, exerting no by-effect upon heart and blood pressure. But there is hardly any harm done by giving those barbiturates which are speedily detoxified and eliminated such as Dial or Didial "Ciba," Soneryl "M & B" or Sodium amytal. But no remedy could possibly be of any avail unless the patient submits to resting quietly on his back, not turning to the side, immovable except for the legs which should be slowly bent and stretched, if necessary passively, to prevent thrombus formation in the veins of the lower extremities, gentle massage of the calves helps in avoiding this complication. During the first few days the diet should consist only of fruit juice, tomato juice, marmite, wheat congee, supplemented later on by mashed carrots, baked apple, toast and a small amount of butter, in non-vegetarians by a soft boiled or poached egg, some steamed fish or boiled chicken, no full meal should be allowed for at least two months. The bowels have to be kept open, if necessary by an enema every other day. Of the greatest importance is to fix exactly when and to which extent the patient is allowed to move (cf. Scherf &

* We are using all the various brands of theophylline ethylene diamine available on the market without finding any difference in their value.

Boyd, 1939) When the first three weeks are over, he may turn slowly to the side which he prefers as sleeping position, by the end of the fifth week he is permitted to sit up in bed, supported by pillows. The decision when he is allowed to leave the bed is fraught with the heaviest responsibility. The following objective findings help in making it: absence of extrasystoles, a systolic blood pressure well over 100 mm Hg, a normal leucocyte count and a normal sedimentation rate, the latter is a very sensitive indicator for the condition of the myocardial infarction and no case of coronary thrombosis should be allowed to get up unless the sedimentation rate became normal. The electrocardiogram, certainly, helps in estimating the progress of convalescence, but the signs of healing which appear after the first three or four weeks develop so slowly that they hardly influence our decision on the bed-side. The earliest possible time for leaving the bed is the seventh week, on this occasion the medical attendant should be present, supervising pulse, heart sounds and blood pressure and framing further arrangements according to these findings. Frequently it will be necessary to keep the patient in bed up to the end of the eighth week and even longer if blood pressure and sedimentation rate make it advisable. It is noteworthy that intensity and duration of the initial pain are in no way indicative of the further course which the case will take, even such patients who hardly felt any pain in the beginning might take a long time to recover. If this kind of management is strictly followed heart failure rarely interrupts the steady improvement. When signs of left ventricular insufficiency should become manifest, such as Cheyne-Stokes respiration, cardiac asthma or restlessness and sleeplessness with a characteristic dry cough during the nights, the failing heart must be supported in spite of the risks involved, the remedy of choice in this condition is strophanthine administered in doses of $1/250$ grain ($1/4$ mg) by intravenous injection, whenever possible this medication should not be commenced prior to the second week following the occlusion, the strophanthine effect begins and wears off sooner than that of digitalis for which reason here the former remedy is preferred. Right heart failure though of a bad portent for the future, does not require immediate treatment, there is no risk in allowing a liver congestion or oedema to develop, on the contrary, the load upon the left ventricle is diminished, the danger of cardiac asthma and pulmonary oedema removed by a weakening of the right heart. In due course, when sufficient time has elapsed for replacing the infarct-

ed area by a firm fibrotic scar which takes six to eight weeks to be formed, digitalis and mercurial diuretics (Mersalyl, "B D H", Neptal "M & B", Esidrone, "Ciba", Salyrgan, "Bayer") will quickly eliminate the retained fluid. One complication exists which urgently requires the right kind of treatment, viz, the appearance of extrasystoles, which almost always are of ventricular origin. Harmless and not needing any treatment, though ventricular extrasystoles frequently are, they have to be suppressed by quinidine medication when occurring after a coronary occlusion, to prevent the development of fatal ventricular fibrillation. Fortunately, in this condition small doses of quinidine sulphate or hydrochloride, 3 grains twice to three times a day, are sufficient for regularising the rhythm, though in many cases repetition of short courses is required. In spite of all efforts a certain percentage of myocardial infarctions does not recover, most of them are cases which have been afflicted by a coronary thrombosis once before or those, occurring in diabetic or syphilitic patients. A sign of bad significance is the development of auricular fibrillation, which should be treated with quinidine.

A few words have to be said on the management of the period which follows recovery. It should be impressed upon the patient that his activities have to remain substantially restricted for at least two years. Some time ago, one would have said that this restriction has to be observed for the rest of one's life, but better knowledge of the clinical picture and, especially, the electrocardiogram revealed that thrombosis not so rarely occurs before the age of 35 (the youngest case in my experience was a Parsee-youth of 19) and that these young men, mostly heavy smokers, might recover to such an extent that for all practical purposes they have to be classified as being cured. Experience derived from such patients, who have recuperated their health almost completely, teaches the all-importance of an extremely regular clock-like way of living and of completely abstaining from smoking, whether a vegetarian or a reasonably mixed diet is used does not seem to make any difference. It is a well known fact that in many cases a coronary occlusion put an end to previous attacks of angina pectoris due to eliminating the stenosed coronary branch from the circulation. Thus, the anginal pain, the danger signal which warned the patient against over-exertion in the stage of mere coronary stenosis is not or not so easily elicited following recovery from occlusion. This absence of pain makes it still more necessary to give detailed advice as to the further

arrangement of every-day life Unfortunately, we are unable to give rules for preventing the recurrence of a thrombosis However, we are of the opinion that in the long run those patients fare best who submit periodically to some treatment, effective either in directly improving the condition of the heart muscle or in achieving the same aim indirectly by dilatation of the coronary arteries To the former purpose twice a year a course of 20 injections of one of the muscle extracts (Corhormon etc) should be given, which supplies the myocardium with adenylypyrophosphoric acid, to the latter, some 10 to 15 injections of theophylline ethylenediamine, administered every 6 months, exert a most beneficial effect Thus, every three months for 3 to 4 weeks the patient is bound to see his medical attendant almost every day which contributes more than anything else to maintaining the required discipline, moreover, four months every year are dedicated to keeping the heart in the best possible condition, to rendering the maximum support, the optimum help which present-day medicine is capable of affording

Finally, attention has to be drawn to some difficulties confronting us whenever a diabetic patient has to be treated who also is suffering from coronary disease This combination is remarkably frequently found, being an open question whether diabetes predisposes to or directly causes damage of the coronary arteries or whether both these conditions develop owing to a common constitutional disposition of the tissues concerned However, clinical experience has taught to be extremely careful in substantially lowering the blood sugar of cases which are liable to anginal attacks, because hypoglycaemia, even of a very slight degree, causes coronary spasm and, thus, brings about myocardial ischaemia and anoxia Moreover, hypoglycaemia in such cases has to be understood relatively to the blood sugar level to which the myocardium or the coronary arteries of the individual patient have been accustomed, a reduction of a fasting level of 200 mg per 100 c c blood to 100 mg already might cause some anginal pain if the coronaries are normally viable These facts have to be kept constantly in mind, especially, if recourse is taken to insulin medication So long as possible in angina of effort and, even more so, in coronary thrombosis the diabetic condition should be controlled by dietetic treatment, giving a sufficient amount of carbohydrates and proteins and restricting the fat intake to a maximum of 100 gm, to avoid the formation of acetone bodies, a very real danger to a weakened heart muscle Only if the fast-

ing blood sugar should remain at a value of more than 180 to 200 mg, the sugar output in the urine exceeds an amount of approximately 25 gm in 24 hours (1.25% of sugar in 2,000 cc of urine) or if aceton bodies should persistently appear in the urine, insulin has to be administered, but even then the minimum doses have to be found which are just sufficient to control the metabolic position, the fasting blood sugar should not be reduced to less than 120 to 130 mg, the urine should never become sugar-free, a safety margin of about 10 gm urine-sugar in 24 hours (0.5% in 2,000 cc) being required to prevent the occurrence of anginal pain due to a too radical insulin effect

The review of the therapeutic facilities which present-day pharmacology, experimental and clinical medicine placed in our hands to relieve the suffering of those afflicted by angina pectoris makes it abundantly clear what a tremendous progress in medicine was achieved since the days of Heberden and Hunter. Although Heberden's genius enabled him to recognize the amazing multitude of clinical features as variations or different stages of one and the same syndrome, a feat achieved without the knowledge of percussion or auscultation, by about one century and a quarter prior to the revolutionary discovery of Roentgen (1895), the ingenious invention of Einthoven (1903), the therapeutic armament of his and his contemporaries was pathetically poor. John Hunter was attended in his illness by William Hunter, Sir George Baker, Sir William Fordyce and, above all, by David Pitcairn, the great clinician who recognized rheumatic fever as an important factor in the aetiology of pericarditis (1788). But all the medication administered by this galaxy of eighteenth century celebrities consisted in emetics, purgatives, blood letting, cupping, application of "a large blister upon the back close to the neck," in sedatives such as valerian, asafoetida and opium and, finally, in oleum succini in various combinations. One hundred and fifty years separate us from these days and mere 75 years from the introduction of amyl nitrite into the therapy of angina pectoris. Though the conditions, underlying this syndrome, are increasing in frequency, especially in the highly industrialized, over-civilized countries of the West, our means of dealing with myocardial ischaemia and anoxia have been multiplied to such an extent that the agonies of pain and anxiety partly could be prevented, partly speedily alleviated and the prognosis considerably improved.

No completeness was intended in surveying the almost unexhaustible subject of this paper. Many features which are to be found in every modern text-book purposely have been omitted to deal in more detail with such facts which uncover the origin of our knowledge, firmly rooted in the past, and those which proved to be of importance in dealing with the practical problems, confronting us every day at the bed-side. To illustrate our indebtedness to the path-finders of previous generation on the one side, to discuss the manifold facilities at our disposal and to ascertain their real value in bringing relief to our patients on the other side, was the aim of these lines.

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RECENT ADVANCES IN THERAPEUTICS

AS INDICATED BY THE TWELFTH 1942 EDITION OF
UNITED STATES PHARMACOPOEIA

By

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A new edition of the British Pharmacopoeia was due, under normal conditions, in 1942. But, in its stead, a series of addenda to the B P 1932 have now been published. The first of these was published, in the ordinary course, in 1936 as a supplement for the interim period, but the subsequent addenda were published in place of the new edition of the B.P. The second and the third addenda were published respectively in 1940 and 1941. The second one authorises the use of certain oils (arachis, cotton seed, and sesame oils which are all indigenous) in place of olive oil which has become scarce, and it also contains cod liver oil substitutes and other vitamin preparations. The only real addition is tetanus toxoid. The third addendum further permits the use of arachis oil in the preparations of certain galenicals and contains new monographs on a number of substances and preparations, mostly German, which were formerly available under proprietary names, such as ateburin, avertin, cardiazol, coramin, doryl, evipan, fouadin, prominal, and uroselectan. It also includes pure vitamin B₁ (aneurin or thiamine) hydrochloride, and a formula for tannic acid paste. A short review of the fourth addendum of 1941 and a note on the fifth addendum of 1942 published in the *Indian Physician* (Vol I, pp 401, and 488, 1942) will give an idea of their nature and scope to the readers. Thus, with the exception of the addition of certain former proprietary preparations, mostly of enemy origin, and some vitamin preparations, the addenda published during 1940-42 are mainly concerned with suggesting substitutes for certain substances now scarce or with the saving of some others, such as alcohol, glycarine, as a war time measure.

During this period of 1940-42, four supplements to the British Pharmac Codex (B.P.C. 1934) have also been published and of these, the first one deals with standards for a number of dressings and the second is concerned with new formulae for a number of preparations. Third supplement, however, contains many new monographs on substances not yet included in the B.P. or its addenda but which have come increasingly in use in recent years. Each monograph also describes the actions and uses of the compounds included in the supplement.

Since there is much co-operation between the bodies responsible for the preparation of the B.P. and the U.S.P., the new edition of the

U.S.P. 1942 may be considered a substitute, in some respects, for the failing new edition of the B.P. The Committee of Revision of the U.S.P. consists of 50 "recognised experts representing almost every field covered by the pharmacopoeia" and the selection of drugs is based upon their intensive discussions and deliberations, so that the U.S.P. provides an authoratively selected list of substances and their preparations having a definitely established therapeutic value in the light of the best current scientific knowledge. "Not only the additions but also the deletions of the new pharmacopoeia represent their decisions. If, in the opinions of at least two thirds of the members of the sub-committee on scope, any of the substances and preparations have become obsolete or have been replaced by more efficient new remedies or preparations, they are refused a place in the new edition. The extent of use alone is not accepted as a sufficient reason for retention of any item. Complex mixtures are also not included. It is not claimed that the final selections are perfect. They may not agree with the views of many able physicians but they are certainly "representative of the best current scientific judgment." Eggleston and Gold advise the practitioners, failing to find the drugs which they have been previously prescribing, to make sure whether the official drugs will not serve them and their patients quite as well or probably even better than their old favourites or those that are not official.

The following brief review of the U.S.P. XII will, therefore, not only indicate the present trend of therapeutics, but also the recent pharmacotherapeutic advances in the "best medical practice of the day." The explanations of the deletions are mostly based on the statements of one of the medical members of the revision committee published in the J.A.M.A. The discussion is arranged according to the predominant action or use of the substances or preparations under review. Their proprietary or trade names are given in brackets.

NARCOTICS, HYPNOTICS, AND SEDATIVES

The different barbiturates (i.e. derivatives of barbituric acid or malonyl urea) differ in their fate in the body and in the duration of their action, so that they can be classified on this basis. To the long acting barbiturates, *barbital* and *phenobarbital*, (called respectively barbitone and phenobarbitone in the B.P.), *pentobarbital sodium* has now been added in the U.S.P. as a representative of the rapidly acting barbiturates. In doses of $1\frac{1}{2}$ to 3 grains given at bed time it can induce sleep with less risk of a protracted hang over the next day, than the older official barbiturates named above. The short acting barbiturates are also employed now for producing intravenous anaesthesia. *Pentothal sodium* which is a thiobarbiturate belonging to the ultrashort acting group has also been added to the U.S.P. *Hexobarbitone* (*Evipan*) is another ultra short acting barbiturate which has been used intravenously for inducing brief anaesthesia and has been added to the B.P. by the third addendum. *Pentothal* is stronger than hexobarbitone and has been recommended for similar purposes in 6% solution and is said to produce rather better muscular relaxa-

tion during anaesthesia and a slightly longer action than hexobarbitone. Another hypnotic added to the USP is *ethyl carbamate (ethyl-urethane)* which has also been added to the BP by the 4th addendum as urethanum. But it is too mild to be used as a hypnotic and has been added for pharmaceutical reasons, to be used to aid the solution of quinine in the preparation of sclerosing solution, a preparation which is also added to the BP by the 4th addendum as well as *injectio sodii morrhuae*. While the three substances of the urea group have been added, *carbromal*, a bromine containing compound belonging to the same group and which was added to the BP in 1932 has been deleted, because it is a "mild sedative and such a limited sedation can be secured satisfactorily with small doses of barbiturates, while the amount of bromine in a dose is too small to give bromide action". At the same time, a bromine containing aliphatic compound now added to the USP is *tribromethanol (avertin)* and its solution in amylene hydrate (avertin fluid). This substance as well as its solution have also been added to the BP by the 3rd addendum and called respectively alcohol tribromethylicum and bromethal. It is used in doses from 0.06—0.01 G per kg body weight for inducing basal narcosis which can be intensified with a volatile anaesthetic to full surgical anaesthesia. Tribromethanol is a white solid, soluble with difficulty upto 3% in water at 40°C. The watery solution is given per rectum, but it easily decomposes on injudicious heating and to avoid this danger it is supplied in solution in amylene hydrate (1cc of the solution contains 1 G).

Two of the inorganic bromides, viz., ammonium and calcium bromides have been omitted from the USP. The ammonium salt has been used because the ammonium radicle is said to be protective to the heart. This belief is fallacious and the salt is also less stable than the sodium and potassium bromides. Both the ammonium and calcium bromides have thus no therapeutic advantage over the alkali bromides and are therefore unnecessary duplicates. Bromides have been used extensively for the treatment of epilepsy and in recent years have been replaced by phenobarbitone (luminal). *Phenitone* (prominal) included in the third addendum of the BP is another barbiturate chiefly used in the treatment of epilepsy, and is said to be superior to phenobarbitone in this respect, because it produces less drowsiness accompanying its anticonvulsant effect. But the effects of diphenyl hydantoin which is also a cyclic ureide allied to barbiturates, show that the two actions are separable, because it is a powerful anticonvulsant and not a hypnotic. Its sodium salt, *diphenyl hydantoin soluble* (dilantin soluble, epanutin, eptoin, solantoin) is now included in the USP and also in the third supplement to the BPC and called phenytoin soluble. According to clinical reports it is more powerful in controlling epileptic seizures than any other drug. It is already recognised as a drug of choice for patients having grand mal or psychomotor seizures. It is most effective in certain types of cerebral dysrhythmia. Different writers have reported various degrees of

success in the use of this new drug Lennox (JAMA 10th Oct 1942, p 452) has recently described it as a sharp edged weapon which must be used both boldly and deftly In severe cases of epilepsy the amount taken daily, 0.3 to 0.6G ($4\frac{1}{2}$ to 9 grains) should be just below the level at which unpleasant symptoms, such as dizziness, muscular inco-ordination, gastric distress, severe swelling of the gums, overactivity, and loss of weight, make their appearance

Opium and its chief alkaloid, *morphine*, are the most important analgesic drugs Pulv ipecac et opii (Dover's powder) which is a two-hundred years old remedy and which was first admitted in the London Pharmacopoeia in 1788, has now been removed from the new USP Its main use is to produce sweating and sleep It is stated that the opium in it is simply "dope" to be better prescribed by itself if it is desired Various derivatives of morphine have been prepared in the hope of finding one that would depress cough without depressing the respiratory centre *Diacetyl morphine (heroin)* was introduced with such claims, but it proved to be more toxic and a more dangerous habit-forming drug than morphine It is no more official Great efforts have been made during the last decade to suppress the traffic in drugs of addiction and to produce a substitute of morphine with its therapeutic effects but without the tendency to produce habit Another alkaloid, naturally present in opium, is codeine which partially satisfies the conditions but it has got little value as an analgesic Chemically it is a derivative of morphine, and no artificial derivative has yet been found which will relieve pain but does not possess the habit-forming property *Dihydromorphine hydrochloride (dilauidide)* which is also a derivative of morphine has, however, been included in the new USP The following table from an expert report to the League of Nations (taken from Clark's Applied Pharmacology) shows the comparative activity and toxicity of morphine and some of its derivatives

TABLE

Showing the comparative activity and toxicity of Morphine and its Derivatives

Drug	Mean therap doses	Relative toxicity	Relative power of producing addiction	Relative analgesic action	Relative depression of Resp and Cough centres	Relative depression of gut movement
Morphine	0.02	1	1	1	1	1
Codeine	0.04	$\frac{1}{2}$	very slight	slight	$\frac{1}{4}$	$\frac{1}{2}$
Heroin	0.005	5 to 10	2-4	2	2	slight
Dilauidide	0.003		$\frac{1}{2}$	1	$\frac{3}{4}$	slight

In man, dilauidide is powerfully analgesic (about 10x more than morphine) but not as powerfully (only 4x) somnifacient This allows its use for the relief of pain with a minimal of hypnotic effects But its toxicity is also greater Its margin of safety is not greater than that of morphine and the duration of its analgesic action is definitely shorter Hence caution, because shorter action will lead to more frequent use Tolerance and addiction occur though addiction does not appear to be so marked Measurement of the

production of the abstinence symptoms showed dilauidide to be much superior to both heroine and morphine. Nausea, vomiting, and constipation are not so marked. Its general dose is one-fourth, or rather one-fifth that of morphine (about 2.0 to 2.5 mgm. as analgesic and half of it as sedative for cough).

Trichlorethylene is used for the relief of pain of trigeminal neuralgia. It is a pungent, sweet smelling, clear, colourless volatile liquid. It is introduced into the new U.S.P. in the form of "pearls" containing it. The pearls are broken and placed in the bottom of a tumbler and the vapour is inhaled until the odour disappears. The treatment may be repeated 3 or 4 times daily for several weeks. Complete relief in a certain proportion of cases of trigeminal neuralgia has been reported. The attacks diminish both in severity and frequency. Its mechanism of action is obscure, but it is likely to be a central depression. But permanency of relief obtained by some without its continued use is unexplained. The disease, however, is likely to exhibit spontaneous remission. Relief is also reported in a certain, though smaller, proportion of cases of *tic dolooureux* and also of migraine. It can produce surgical anaesthesia, when sufficient amount is inhaled but there is no advantage or any special indication for its use as a surgical anaesthetic.

The new U.S.P. describes two qualities of ether. One called "ether," is meant for anaesthesia and the other is "ethyl oxide" or solvent ether. More rigorous tests for purity are applied in case of "ether" which is the only one to be used for anaesthesia. Peroxide formation was formerly fairly rapid in ether and there was an impression that ether deteriorated on exposure to air. It was, therefore, stored in well-closed small containers and was not used for anaesthesia if the original container was opened longer than 24 hours. But scientific studies have now shown that anaesthetic ether can be sold safely in large containers, because new methods have been developed which avoid the formation of peroxides. The metal containers in which anaesthetic ether is now supplied in U.S.A., are of very high quality and ether stored in them retains its purity for weeks and months, even if the seal is removed and the container stoppered with cork. The safety of bulk ether for anaesthesia thus appears to be established and, therefore, official ether for anaesthesia may be stored in containers as large as (and upto) 3 litres, with a lot of saving in material and cost. In small hospitals and establishments where the bulk package may not be utilised in six months or more there is danger of its being peroxidised towards the end of the period and here the use of bulk ether would not be advisable.

CENTRAL NERVOUS STIMULANTS

Of these *leptazol* (*cardiazol*) and *nikethamide* (*coramine*) which have been added to B.P. by the 3rd addendum have not found a place in the U.S.P. But *picrotoxin* has been accepted. It has been found to be effective as a stimulant to respiration which had been depressed by certain narcotics. In animals, remarkable antagonistic

action has been observed between barbiturates and picrotoxin and during the past few years picrotoxin has been successfully used in the treatment of barbiturate poisoning. These comatose patients can tolerate relatively very large doses of the substance which are toxic in the normal individuals. It is the practice in barbiturate poisoning to give 5 to 10 mgm intravenously or intramuscularly, such doses being repeated every $\frac{1}{2}$ to 1 hour, until signs of stimulation appear. Cases have been reported of patients receiving 200 to 300 mgm of picrotoxin in 24 to 48 hours.

AUTONOMIC DRUGS

The sympathomimetic substance, *amphetamine* (benzedrine) is now accepted in the U S P. It is a synthetic substance chemically and pharmacologically related to adrenaline and ephedrine, but it is a powerful central stimulant. Its analeptic effects have not yet been fully investigated. It is, however, employed for its central action in the treatment of narcolepsy and certain depressive psychopathic conditions, and also in postencephalitic parkinsonism in conjunction with scopolamine. But it is more commonly used for its peripheral vasoconstrictor effect in the upper respiratory passages in the form of a 1% solution in liquid paraffin. The base itself (as well as its carbonate salt) is volatile and is also used by inhalation, but, in this form, it should not be used too frequently, otherwise it would cause central stimulation and excitement. Its non-volatile sulphate salt which is also included in the U S P can be administered orally as well as by injection. Both amphetamine and its sulphate salt are also added to B P by the 3rd addendum. Amphetamine sulphate has been used with homatropine as a cycloplegic. Homatropine itself produces some cycloplegia as well as mydriasis, but *eucatropine hydrochloride* (euphthalmine) which is now included in the U S P produces mydriasis without cycloplegia. Its mydiatic action develops slowly than that of homatropine and it is also used in stronger solution (5—10%). Another autonomic drug added is *neostigmine hydrobromide* (prostigmine), the synthetic substitute of physostigmine or eserine. Neostigmine has relatively a more powerful action on the gut than on the heart so that its effective dose (0.5 mgm) can be used for the treatment of intestinal atony and for post-operative retention of urine without the occurrence of any side-effects on the circulation. It has also been employed successfully in the treatment of myasthenia gravis. *Neostigmine methyl sulphate* is another salt admitted in the U S P. A choline ester, carbachol (doryl) now admitted to the B P in the 3rd addendum did not find a place in the U S P. It also increases muscular power in myasthenia gravis but neostigmine remains the drug of choice. Another substance used in myasthenia and also in myopathic dystrophies and now added to the U S P, is *aminoacetic acid* (glycocoll, glycine) which is given in daily doses of 15—30 gms. Its value is, however, considered doubtful and better results are stated to be produced by the combined treatment with neostigmine. The exact mechanism by which it exerts its effects on the muscular con-

traction is also not understood, and varied explanations have been given for the clinical improvement seen during its use

LOCAL ANAESTHETICS

Three new drugs, *viz.*, butaprobenez sulfate, tetracaine hydrochloride and butesin (with its picrate salt and its ointment) have been added. *Butaprobenez* (butyn) is chemically related to procaine (it contains one more c in the ester group). It has largely replaced cocaine for surface anaesthesia in the eye, nose and throat. It is said to be even more than or as powerful as cocaine, but it does not constrict blood vessels (therefore probably on subcutaneous use it is more toxic than cocaine), causes no mydriasis (an advantage in operations on the iris), and causes less damage to cornea. The solutions of the sulfate salt usually 2% can be sterilised by boiling. Its action is prompt as well as sustained. *Tetracaine* (pantocaine) hydrochloride resembles procaine in its action but is more efficient as a surface anaesthetic on mucous membranes. A 0.5% solution is used for the eye, 2% in the nose and throat and 1% for spinal anaesthesia, the dose is 1—2 c c or 10—20 mgm. *Butesin* belongs to the group of insoluble local anaesthetics (like orthocaine, etc.) and its picrate salt incorporates the anaesthetic properties of butesin with the antiseptic properties of picric acid. It is recommended in the treatment of burns, ulcers and other denuded painful lesions of the skin. 1% ointment is used.

DIGESTIVE SYSTEM

Gastric antacids are used extensively in the treatment of hyperchlorhydria. These drugs may be classified in two ways. *Firstly*, into systemic and non-systemic antacids. The non-systemic antacids form compounds which are not absorbed and are much less prone to cause alkalosis. *Secondly* they can be classified according to whether they act by chemical action (with the acid) or by physical adsorption (like many colloidal substances). The adsorbents do not cause alkalosis. In the alkaline intestinal contents the bound acid is freed again to be neutralised to form sodium chloride which is absorbed. Four new antacids or anacid preparations are described in the USP XII. Of these *magnesium trisilicate* has now been added to the B.P. by the 4th addendum. It is an insoluble powder which in the stomach becomes gelatinous in consistency and reacts slowly with the hydrochloric acid there, with the formation of magnesium chloride and hydrated silicon dioxide. The magnesium chloride reacts again in the intestine to form magnesium carbonate, which is eliminated in the feces, and sodium chloride which is absorbed. The colloidal silica acts as an absorbent. The gelatinous consistency of the preparation also allows an adherent protective coating. Thus it is an adsorbent as well as antacid, yet excess of it will not render the stomach contents alkaline nor does it cause alkalosis or toxic symptoms. Two other preparations are *aluminum hydroxide gel* (magma or cream) and *dried aluminum hydroxide*. The former is a more effective adsorbent. It is now included in the

B P C supplement In the colloidal form it acts rather as a physical than as a chemical agent, the reaction being chiefly adsorption of the hydrochloric acid, but there is also some slight chemical neutralization, the small amount of aluminium chloride formed acting as an astringent. It also absorbs toxins, gases and enzymes but it is not found to affect the digestion and absorption of food. It produces no systemic alkalosis and as a colloid it acts as a protective demulcent. There are no toxic side actions, except that it is said to be slightly constipating. The fourth preparation is *tribasic magnesium phosphate* (tablets)* already included in the B P C Supplement. It has enjoyed a certain repute as a moderately effective antacid which produces no systemic alkalosis. But its gritty character has been found to be an undesirable property.

The following preparations acting on the digestive system have been deleted from the U S P and the reasons given for their omission are stated with their names below.

Cinchona is no longer employed as an antimalarial. For the purposes of a bitter other remedies just as effective but simpler are available. *Serpentaria* which was a pharmaceutical necessity in compound tinct of cinchona has therefore been deleted. Pepsin is omitted because it is superfluous in therapeutics. For the digestion of proteins it acts in acid medium and in gastric reflux the needed acidity cannot be obtained in the stomach by any doses of acid that is possible for a patient to swallow. Compound powder of Senna (pulv. glyceric. co.) is deleted because as a senna preparation it is complicated by the presence of sulphur which gives an unduly soft consistency to the stools and often very offensive odour. *Podophyllum* is omitted because the drastic cathartics no longer have pharmacological approval. They are irritant to the whole alimentary tract. If catharsis fails to take place they are capable of producing inflammation of the intestine and after absorption, of the kidneys. Acetyl tannic acid and albumin tannate have not proved efficient as intestinal astringents. Neither tannic acid nor gallic acid appears in the feces. Bismuth subgallate which is now added to the B P by the 11th addendum is deleted because it has no advantage over the subcarbonate. Because of the presence of the gallic acid it has produced the erroneous idea that it is astringent. Known as a tannic acid remedy does not reach the lower intestine as such. Tannic acid and its preparations are to be preferred to nutgall and its preparation. Two local irritants, cantharis and capsicum have been omitted the former because therapeutic blistering has fallen into disuse and as an irritant in scalp lotions and otherwise it is superfluous. Capsicum is not considered important enough for the pharmacopoeia. Solution of iron tersulfate formerly used as a haemostatic has been omitted because it makes a nasty mess when mixed with blood and is locally irritant, even corrosive. Iq fern perchlor is required for the preparation of tinct ferr perchlor which is largely supplanted as an antianæmia remedy, by iron preparations which do not injure the teeth and are less astringent. Both the liq and the tinct are therefore deleted.

Normal human blood, citrated human plasma, as well as the sterile sodium citrate solution, all used in (blood) transfusion have been given a place in the new U S P.

THE CIRCULATORY SYSTEM

The crystalline cardiac glucoside, ouabaine obtained from *Strophanthus gratus* has been added, because of its well defined physical characteristics, it has served as a standard in the USP for the assay of the digitalis group of drugs. *Strophanthin*, which is an amorphous mixture of water soluble glucosides obtained from other species of *strophanthus* has, however, been retained. *Strophanthin* has a place also in the B P 1932. While ouabaine has been added to the USP, squill has been deleted because it is stated to lack the highest approval as a cardiac drug and its use as an expectorant is based on erroneous observations. The B P commission, however, does not consider squill to be dispensable and the 5th addendum provides for the use of Indian squill (*urginea*) instead of Mediterranean scilla.

* Instead of this, tribasic calcium phosphate (dose 15 grains) is mentioned in their review by Eggleston and Gold, with the remarks that it not only acts as an antacid but also as a useful source of calcium and phosphorus. This is of importance in view of the recent evidence that aluminium hydroxide may precipitate the non absorbable alumin. phosphate and thereby deplete the body of phosphorus stores, leading to phosphorus deficiency.

In addition to strophanthin and ouabain which are useful for parenteral administration the new U S P also includes a digitalis injection described as "purified mixture of digitalis glucosides" It may be added here that digoxin, a glucoside from digitalis lanata useful for parenteral administration has been also added to the B P by the 4th addendum Moreover, the frog method of standardisation of digitalis preparations in the previous edition has now been replaced by the cat method in the new U S P because extensive clinical experience and special experiments have shown that the results by the cat method more nearly represent the relative potency of the preparations for human beings Furthermore the digitalis preparations are to be assayed against a digitalis reference powder, 0.1 G of which is defined as 1 U S P unit (It would represent approximately 1.3 "cat units")

Aconite and its tincture have both been deleted because in fever it has been supplanted by strikingly better remedies As a vagus stimulant it is not employed, probably because of its lack of certainty or its lack of safety in the necessary doses The tincture has already been omitted from the B P but the liniment is retained for external use

ANTIPYRETICS AND DIAPHORETICS

A deletion of Dover's powder has already been mentioned The solution of ammon acetate and the spirit of nitrous ether, both common constituents of diaphoretic mixtures have been deleted, because the former is believed to be of no therapeutic value and the latter is neither effective as a nitrite nor has it any distinctive therapeutic properties On the other hand the 5th addendum to B P provides for a concentrated solution of ethyl nitrite to save alcohol Spirit of chloroform is another spirit omitted because it is not desirable as a sedative and not needed as a carminative

(To be Continued)

Continued from p. 238

Book Reviews & Notices

Dr Grant has many stringent things to say about the health policy of the Government of India The state cannot keep on blaming the individual for his ill health

In the past states regard the primary necessities of life—food and living conditions—as responsibilities of the individual but to day progressive states recognize the need for providing such necessary services as one is unable to obtain as an individual This is fundamental to modern organized life Included in these is the right to food and everything necessary to maintain health

Dr Grant has to make many concrete proposals to improve the present conditions, *eg*, (1) Consolidated Public Health Acts, (2) scientific training and supervision of the social services, (3) better central and provincial planning, and (4) the training of an adequate number of doctors, nurses and health visitors The word planning occurs several times in the pamphlet but who is to plan and for whom?

'Doubtless a people gets the health as it gets government which it deserves An individual cannot be said to be alic at all certainly he cannot be healthy or happy without certain basic needs such as enough of the right food decent shelter a job of work under suitable conditions, opportunity for play and access to sunshine and fresh air Without these simple things health and happiness are a mirage To preach health to the underfed is hypocrisy —Horder

Critical Notes and Abstracts

IODIZED CAFFEINE IN THE TREATMENT OF BRONCHOSPASTIC DYSPNOEA AND IN CHEYNE-STOKES RESPIRATION

Wendkos and Robertson (*Internat Clinics*, June 1941, p 68) have treated bronchial asthma and Cheyne-Stokes respiration with caffeine in organic combination with iodine with considerable success and without any unpleasant symptoms which are so common with the use of adrenalin or ephedrine. There were no symptoms of iodism or other unpleasant side reactions even after prolonged use of iodised caffeine nor was there any insomnia. On the contrary the patients slept better, especially those suffering from left ventricular failure. None of the patients became refractory to the treatment. Patients who were refractory to adrenaline, responded to its use after taking iodized caffeine for a few days. Caffe-iodine—an additional product of trimethylxanthine with sodium iodide, consists of caffeine in organic combination with iodine. Each fluid ounce of this preparation is equivalent to 6 grains of caffeine alkaloid and 12 grains of sodium iodide. The dose is one fluid drachm three or four times a day i.e. 3 grains of caffeine and 6 grains of sodium iodide in a day. The authors summarise their clinical experience in the use of this drug as follows:

- 1 There is accumulated evidence that xanthine compounds and iodides are effective bronchodilators and respiratory stimulants.

- 2 An iodized form of caffeine when given orally has been found effective in abolishing bronchospastic dyspnoea and Cheyne-Stokes respiration when it is secondary to uncomplicated left ventricular failure.

- 3 Iodized caffeine would appear to be the drug of choice in the treatment of bronchial asthma when associated conditions such as diabetes, myocardial disease, or hypertension would contraindicate the use of sympathicomimetic drugs.

- 4 Iodized caffeine possesses none of the unpleasant side reactions, harmful properties or other disadvantages of adrenaline or ephedrine.

- 5 Iodized caffeine has been found effective in asthma when the other bronchodilator drugs have failed to be of benefit.

- 6 The effect of iodized caffeine in Cheyne-Stokes respiration is comparable with that of aminophylline.

L I I

NICOTINIC ACID IN ASTHMATIC PAROXYSMS

F E Maisel and E Somkin (*J Allergy*, 1942, 13, 397) have published a preliminary report on the treatment of the asthmatic

paroxysm with nicotinic acid. They found that (a) severe asthmatic attacks were controlled within 3 to 5 minutes, and improvement lasted 3 to 15 hours, in 16 of 21 patients by the intravenous injection of 0.1 g of nicotinic acid, (b) 5 of 9 chronic asthmatic patients were benefited by 0.2-g doses given orally three times a day before meals and on retiring, and (c) 11 of 18 patients receiving intravenous therapy followed by oral therapy showed decided improvement in their asthma. The patients experience a flush and a sensation of heat, then often begin to cough, and expel tenacious mucous plugs. The beneficial effect is thought to be produced by the strong vasodilator properties of nicotinic acid, relieving the bronchospasm or directly affecting the pulmonary vessels and has no bearing on vitamin deficiency. The patients were mostly beyond middle life, often with a well-marked infective element and not responsive to ordinary anti-allergic methods of therapy. No patient developed any disturbing symptom.

THE SYNDROME OF PAINFUL DISABILITY OF THE SHOULDER AND HAND AFTER CORONARY OCCLUSION

Askey (Am Heart Jour July 1941) describes a syndrome of painful disability of both shoulder and hand which persists for several months to one or two years after coronary occlusion. This is not the same as the pain in left arm and hand after a paroxysm of angina pectoris when the extremity is held immobile for fear of exciting more pain. The syndrome consists of a persistent painful disability which is associated with restriction of shoulder movement and swelling of the fingers.

Askey has observed 23 patients, ranging in age from 48 to 79. In all the pain came on after coronary occlusion, except in six patients who had previous upper extremity pain which became aggravated after the cardiac attack. The condition resembles acute or sub-acute peri-arthritis of one or both shoulders, followed usually in days or weeks by stiffness, pain, and swelling of one or both hands. The shoulder involvement is associated with painful restriction of arm abduction and external rotation.

The onset of pain may coincide with the occlusion and it may be of excruciating intensity, requiring morphine, with marked trapezial tenderness, or it may appear several weeks after the cardiac seizure and be mild, localised to the deltoid area and attributed, perhaps, to a hypodermic injection. The disability of abduction and external rotation lasts for over an average six months. Within a few days or weeks, there appears a mild unilateral or bilateral pain in the hands, with stiffness and inability to close the hand. This stiffness grows quickly worse, the finger joints become swollen, and the skin becomes tense and glossy, with obliteration of the interpalangeal wrinkling. In severe cases the hand is fixed in extension. There is often a deep rose red suffusion of the palms.

The clinical condition of the shoulder and the hand suggests a rather rapid development of arthritis with a very gradual improvement. The purplish red discolouration and oedema of the hand similar to acrodynia suggest the prominent part the sympathetic innervation plays in the production of the syndrome.

In some patients, after a few months, there is a distinct thickening of the palmar aponeurosis, near the metacarpophalangeal junction, usually of the middle and ring fingers, the overlying puckered thick skin resembling the early stage of Dupuytren's contracture.

During the stage of shoulder pain, in some patients, there is a point of localised tenderness situated over the anterior border of the trapezius muscle upon the mesial angle of the superior border of the scapula. Pressure over it produces severe pain. The point apparently corresponds to the site of the trapezius branches of the cervical plexus. The brachial plexus was not actually sensitive to pressure.

Libman et al have reported that the pain of subacromial bursitis may be relieved by pressure against the spine at the level of the angle of the jaw. In certain cases Boas and Levy were able to relieve the shoulder pain which followed coronary occlusion by pressure on the brachial plexus. Edeiken and Wolferth described a trigger zone over the upper border of the left scapula where pressure induced pain in the left shoulder and up over the left side of the neck.

This shoulder pain and disability are not amenable to any form of treatment. Cobra venom, bee venom, large doses of thiamin, salicylates and paravertebral alcohol injection, all have a negligible effect. The removal of septic foci, if any, does not affect the pain in any way. Heat, which is intolerable at the early stages, seems to help later, in conjunction with gentle massage.

The syndrome is a sequel to coronary occlusion. If it occurs in the absence of an attack of acute occlusion, silent occlusion should be suspected and an electrocardiogram taken. The syndrome seems to be common in persons with latent arthritic changes. The pathological process is self-limited and little affected by any therapy. It appears to be the resultant of sympathetic nerve disturbance caused by myocardial ischemia and preexisting shoulder and hand lesions.

N D P

HYPERSENSITIVE CAROTID SINUS REFLEXES

The carotid sinus is a bulbous dilatation of the first portion of the internal carotid artery with a rich and complicated nerve supply. It receives nerve branches from the glossopharyngeal nerve, the vagus and the cervical sympathetic, and occasionally a few branches from the hypoglossal nerve. It is believed by some that the major nerve supply is from a branch of the hypoglossal nerve, the nerve of Heering.

The symptoms of hypersensitive carotid sinus reflexes, or as it is sometimes called, *carotid sinus syndrome*, consist of spontaneous

attacks of unconsciousness and vertigo. The syncopal attacks may or may not be associated with convulsions or convulsive movements. The attacks usually last from a few seconds to several minutes. Occasionally they may be precipitated by turning the head suddenly, looking upward, stooping, changing the position of the body quickly or by pressure on the carotid sinus. In most instances the precipitating factors in the spontaneous attacks are not known. A definite aura is usually present, which consists of weakness, light-headedness, spots before eyes, and a sensation of distress in the epigastrium, the patient feeling as though he were going to faint. During the syncopal attacks, the patient may turn pale, perspire, often profusely, and fall. Very rarely will he bite his tongue, or lose control of his sphincters. The attacks nearly always occur when the patient is sitting or standing, and rarely when he is lying down. The frequency and severity of the spells vary greatly, as they may be mild and occur infrequently or may be severe and occur frequently, many spells occurring in one day. The light spells are very similar to petit mal seizures. The syndrome is more common in middle-aged and elderly persons, being rare among young persons, although it may occur. The diagnosis is made from the history and by inducing an attack by making pressure over one of the carotid sinuses. It is not necessary and it is not advisable to make pressure over both carotid sinuses at the same time.

Carotid sinus syndrome may be associated with other clinical conditions such as organic heart disease or Meniere's disease, when the diagnosis may become quite difficult.

The treatment of the carotid sinus syndrome may be roughly divided into three groups. (1) Where the symptoms are mild and the attacks occur at infrequent intervals, no treatment is required other than reassurance. (2) Where the symptoms are moderately severe and the attacks occur more frequently, the patient should be instructed to avoid turning his head quickly, looking upward and stooping suddenly. He should avoid any constriction about the neck. If the spells are quite severe and occur at intervals sufficiently close to interfere with the patient's work or activity, then medication is indicated. Many drugs have been used for this malady, the commonly recommended being phenobarbital, ephedrine, epinephrine, benzedrine, atropine and dilatin. The drug treatment is not particularly satisfactory. Phenobarbital gives the best results. (3) Where the attacks are severe and a thorough medical course of treatment has been carried out without success, operative treatment is indicated.

—Craig and Smith, Mayo Clinic

Book Reviews and Notices

THE HEALTH OF INDIA by John B Grant, M.D., M.P.H., published by Oxford University Press, Bombay, 1943, p 32, As 4

This pamphlet No 12 in the series, Oxford Pamphlets on Indian Affairs, is written by Dr J B Grant, the Director of the All-India Institute of Hygiene and Public Health, Calcutta. It gives a concise and an admirable account of the present state of the health conditions in India and makes concrete suggestions for its improvement.

The account of the present state of health affairs makes a sad reading. After a century and half of the British Imperial Rule the author has to begin his pamphlet with these words —

"The level of health in India is low. Preventible epidemic diseases such as smallpox, typhoid, dysentries, cholera and malaria are widespread. Out of 6,165,234 deaths in 1939 in India accounted for 1,411,611 smallpox for 18,101 cholera for 97,566 and dysentries and diarrhoeas for 260,300. Tuberculosis is spreading and each year presents a more menacing problem. The resistance of the population to disease is low. Malnutrition and nutritional diseases are omnipresent. These in part account for the anaemia which is particularly widespread among women and children."

India has the highest mortality rate, the highest birth rate and the highest infant mortality rate (22.4, 34.5, and 162 per thousand respectively, the figures for England being 12.4, 14.9, and 58), amongst the civilized countries. The expectation of life in British India is stated to be 27 years, in contrast to 67 years in Australia, 63 years in England and 47 years in Japan. This state of affairs is due to a low standard of living, lack of education and administrative inefficiency. When one sees what Japan has achieved in 40 years or what Russia has done in a short space of 15 years, (see *Socialised Medicine in Soviet Russia* by Henry Sigerist), it is not difficult to locate where the fault lies. The rulers' claim that India has been freed from wars, epidemics, and famines, is a false one. What is happening in Bijapur at present will open our eyes. In fact large parts of India are virtually in a state of perpetual famine. As to the epidemics one does not yet know their natural history completely and the part played by the human agency in their control.

"Pestilence has become an old-fashioned word. Most of the great plagues have shrunk into the background of time. Is this our doing? Only in part. Leprosy, plague, typhus, and tuberculosis began to recede because of cloudy biological trends or broad social changes, not because of deliberate control. Syphilis still uncontrolled seems to have lost some of its severity. Malaria, along its geographic frontiers has yielded to the farmer rather than the epidemiologist. Cholera has probably shot its bolt before we learned how to hold it at bay. We have been harrying a retreating enemy, and building defences against his return." (Geddes Smith, *Plague on us* 1941)

As to the medical education the record is as deplorable. It is now a hundred years since the western medicine was introduced in India to supply the needs of the army, not of the people and a more sterile century it is difficult to find elsewhere, in the history of medicine. There are 42,000 doctors for the needs of the teeming millions of India. There are more doctors in Japan with a population a little more than that of Bengal. There are 4,500 nurses in the whole of India, one nurse for 10 doctors. In Great Britain there are 61,420 doctors and 109,500 nurses or approximately two nurses to each practising doctor. This state is inevitable till the whole educational and health policy of the Government is altered.

(Continued on page 233)

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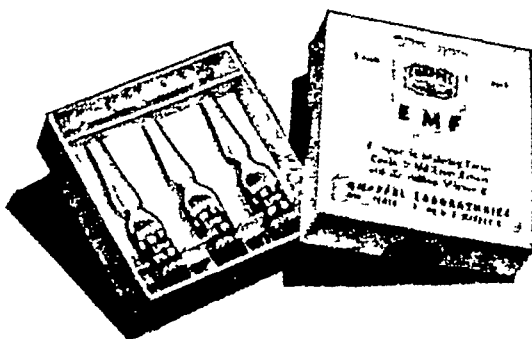
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The Indian Physician

VOL II NO 7

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Original Contributions

LIVER FUNCTION TESTS

By

N D PATEL

M D (LOND), M R C P (LOND), F C P S (BOM)

ANATOMICAL DIAGNOSIS & FUNCTIONAL DIAGNOSIS

A mere anatomical diagnosis is rarely sufficient in clinical medicine. It is not enough to know the variations in size, shape, or position of an organ. One should get a clear idea about functional efficiency, both absolute and relative, of the organ concerned and also its latent reserve power. This conception of functional diagnosis was introduced in clinical medicine by Rosenbach as early as 1878 and 1891. It has been successfully worked out in cases of such important organs as the kidneys, the stomach, the pancreas, and the heart and special tests estimating the functional efficiency of these organs are a routine clinical practice. But this is not so in the case of the liver. There are few physicians and still fewer surgeons who ask for estimation of hepatic efficiency. A surgeon who will not touch a patient with a cardiac murmur, albuminuria, or glycosuria before the functional efficiency of the heart, the kidney or the pancreas is estimated, will not hesitate to operate on a patient with a chronic gall-bladder disease without deciding on the status of the liver. A physician goes on using hepatotoxic drugs such as the organic arsenicals, the sulfonamides, alcohol, carbontetrachloride, cinchophen, etc., till there is clinical jaundice. Even in the presence of marked hepatic failure such as cirrhosis of the liver with ascites his use of mercurials is not guided by any rational view of the functional state of the hepa-

A paper read before the Medical Congress of the independent medical profession and members of the Army Medical Service held on the 12th June 1943 at the Grant Medical College Bombay

tic parenchyma The argument is that there are no reliable hepatic function tests During the last thirty years or so a number of tests have been devised to estimate the efficiency of the liver but few have proved physiologically and clinically sound Most of the tests have only their authors as supporters. Some, based on unsound principles, have not been repeated by others Other tests, better devised, have been worked out by several investigators but have not proved useful in clinical practice The reasons for this are many *First*, the multiplicity and dissociation of hepatic functions No single test of liver function can give information about all the functions of the liver A search for such an all-embracing single test of liver function is doomed to fail It is in the nature of the hepatic physiology that there must be several tests of hepatic function *Second*, the enormous size and the relatively high reserve power of the liver The conception of non-functioning nephrons and neurones which become active only when there is renal or nervous damage has been accepted in renal and nervous physiology Similarly there must be millions of units of hepatic cells which come in action only when the organ is damaged Recent experiments on animals have shown that as much as 4/5 or 5/6th of the liver tissue must be removed before evidence of hepatic insufficiency is obtained Experiments to produce obstructive jaundice by bile duct ligation and to produce parenchymatous injury by carbon tetrachloride have also shown the necessity of wide spread and diffuse changes in the liver before clinical evidence of hepatic failure is recognised by the hepatic function tests. This suggests that the liver function tests are of possible importance only where the lesions are wide-spread and diffuse throughout the liver They are likely to be negative in the presence of slight or only localised affections *Third*, apart from its enormous reserve power, the liver has great power of regeneration The nodules of rapidly regenerating liver cells after parenchymatous hepatic injury are all functionally active units and the liver function tests may be negative for a long time in the presence of sufficient regenerated tissue

HEPATIC FAILURE

Hepatic failure or insufficiency is not a simple disorder The multiple functions of the liver do not fail at once or all together There is a dissociation of functions and only one

function may be affected while others may remain normal for a considerable time. More than one test, and because of a high degree of hepatic reserve a proper interpretation of the tests carried out in conjunction with the clinical finding is necessary in arriving at conclusions regarding the functional efficiency of the liver. Again, it must be remembered that a number of laboratory tests are diagnostic tests of hepatic injury or specially helpful in differentiating intrahepatic jaundice from extrahepatic jaundice and are not real tests of hepatic function. Physiologically, failure of hepatic functions may lead to (1) cholaemia failure of excretory and detoxifying functions, (2) cholorrhoea, post-operative excessive secretion of chloride and base by the liver, (3) hepatic coma, disturbed glucose metabolism and possible deficiency of vitamin B complex, and (4) hæmorrhagic tendency, failure of the liver to form prothrombin. Clinically the manifestations of liver disease form four well defined syndromes —(1) disturbances of bile secretion and excretion, (jaundice), (2) alterations in the size and shape of the liver (hepatomegaly or atrophy), (3) portal obstruction, (ascites and oedema), and (4) hæmorrhagic tendency. Recent work with liver function tests has brought to light the surprising frequency of two more states, one, that of subclinical or unrecognised liver damage or a state of latent hepatic dysfunction, and the other, a state of constitutional hepatic inferiority or a "weak liver". Unrecognised liver damage has been demonstrated in a number of cases of chronic disease of the biliary tract and also in cases of acute hepatic trauma or crush injury, hyperthyroidism, burns, intestinal obstruction, and in many other diverse pathological states. A study of post-operative deaths has resulted in the conception of hepatic and hepato-renal syndromes. "An explanation advanced for this syndrome postulates an underlying hepatic damage or dysfunction which becomes progressively more pronounced when the strain of surgery is put upon it. The damaged cells of the liver failing in their function, release into the circulation some toxic substance which is excreted in the kidneys but which is so potent that the convoluted tubules, unfitted by nature for such a load, break under it. The ultimate cause of the liver and the liver-kidney deaths is an inherent or acquired weakness of the liver cells which exists as a subclinical disease which is present far more frequently

than is generally suspected, and which can often be demonstrated by hepatic function tests" (Boyce, 1941) A study of liver function tests and their co-relation with the histological study of the liver has shown that the prevalence of liver disease in the presumably healthy subjects is as striking as the marked degree of hepatic involvement associated with pathologic gall-bladders Such histologic demonstrations should make it easy to accept laboratory evidence of impaired liver function in the absence of clinical evidence It is necessary to identify individuals with constitutional hepatic inferiority because of the risks to which they are exposed They require a special protection against hepatotoxic drugs and certain types of anaesthetics and operations These subjects with vulnerable livers probably know more about their "weak livers," from the experience of biliousness, flatulence, allergic states, causeless vomiting, or headaches, than their medical attendants

LIVER FUNCTION TESTS BILE METABOLISM

Van den Bergh Test The van den Bergh test is a reliable and very practical test if used intelligently The estimation of serum bilirubin is comparable with the estimation of blood urea in cases of renal disease Normally there is 0.1 to 2 mgm of bilirubin per hundred cubic centimetres of serum Any increase in this amount is due to (1) excessive production (haemolytic jaundice), or (2) failure of liver cells to excrete it as a result of parenchymatous injury (hepatogenous jaundice), or (3) reflux of bilirubin into the blood from obstruction to the larger bile passages (obstructive jaundice) Pure forms of jaundice are probably rare and all types are mixed Still this classification of jaundice is clinically very helpful and there is little advantage in replacing it by the newer division of retention and regurgitant jaundice The indirect van den Bergh indicates that the blood bilirubin is the pigment which the liver has not been able to remove from the blood stream It is "bound" in some way in blood and cannot be excreted by the kidney Hence there is acholuria The amount of bilirubin in the blood is never more than 4 to 8 mg per 100 cc of serum When the value of indirect-reacting bilirubin is above 4 mg per 100 cc of serum functional impairment of the liver cells is assumed The direct reaction means that the whole bile has been regurgitated into the blood stream, and that the underlying patholo-

gical process is either an obstruction of the bile ducts or rupture of the canaliculi with necrosis of the liver cells. The serum bilirubin may be as high as 50 mg per 100 cc of serum. Van den Bergh is thus a simple and good test of liver function though not a very sensitive one. A direct positive reaction indicates marked degree of liver damage in about 85 per cent of the cases and in a rather smaller number of cases in which the reaction is indirect.

Icteric Index The measurement of the degree of bilirubinemia is a simple and an accurate test and may be used to detect subclinical or latent jaundice and to record fluctuations in the intensity of jaundice which cannot be detected by clinical observation. The curves plotted from serial tests are very useful in the differential diagnosis of jaundice. Icteric index determined by Meulengracht method has 4 to 6 units as normal, by Newberger acetone method 2 to 5 units as normal. The values above these are pathological, and often comparable with other tests of defective function but it is not a true test of liver function.

Urobilinogen Determinations The presence of urobilinogen in urine is a sign that the liver is damaged and it is unable to resynthesise it into bilirubin. Its complete absence in the feces and urine is a sign of complete biliary obstruction. There are difficulties about its quantitative estimations and only qualitative tests are used. Again it is excreted intermittently during the day and several fresh specimens must be examined. It is said to be a very delicate single test of hepatic function. If it is present in dilutions greater than 1:20 it may be assumed that the liver damage is extensive. To 10 cc of fresh urine 1 cc of Ehrlich's aldehyde is added and the test tube warmed. Rose colour appears if urobilinogen is present, and the amount is determined by diluting the specimen and observing the dilution at which the reaction is still present.

EXCRETORY FUNCTION

The Dye Tests Isoiodoquin, rose-bengal, bromsulphthalein, and azorubin S are some of the dyes used to estimate the liver function. Bromsulphthalein is considered to be 96 per cent accurate. A dose of 5 mg per kilogram of body weight, is injected and a single specimen of blood is taken at the end of one hour. The amount of the dye in it is determined by transverse com-

parison of the serum with standard tubes in a colorimeter. Retention of the dye of more than 5 per cent is considered significant. Retention above 12 per cent is taken as a definite evidence of hepatic injury. *The Serial Dye Test* is a modification of this test to overcome some objections. Here the rate of excretion is noted by taking the blood specimens every 2 minutes for 30 minutes through a special needle with a 3-way valve. The amount in each specimen is estimated and a graph prepared. *Azorubin S Test* is said to be still superior in relatively early cases of hepatitis. Here after the injection of the dye the time taken by it to appear in the duodenal contents is noted. The normal appearance time is 15 to 30 minutes. The dye tests are not useful in the presence of jaundice. *Bilirubin Tolerance Test* is comparable to carbohydrate tolerance test of pancreatic function. It is an index of the excretory function of the liver. A measured amount of bilirubin is injected in the vein and the icteric index is measured before the injection and at definite intervals after the injection. A retention of more than 5 per cent is considered abnormal. This is considered a very reliable and sensitive test of liver function and is used extensively.

CARBOHYDRATE METABOLISM

Galactose Tolerance Test. A normal man does not excrete more than 2.5 to 3 g of sugar in the urine in the 5 hours immediately following ingestion of 40 g of galactose. In the presence of hepatic injury, the conversion of galactose into glycogen and its storage fail and more than 3 g of sugar appears in the urine. A positive test is a sign of parenchymatous damage, and it is useful in differentiating obstructive from hepatogenous jaundice, but only in their early stages. It is not a reliable test of liver function.

Levulose Tolerance Test. 50 g of levulose (as a war time measure honey is recommended in its place) is given orally and the blood levulose is estimated at 30 minute intervals for 2 to 3 hours. A normal curve shows a maximal rise of not more than 20 mgm of levulose per 100 cc of blood, within an hour of ingestion of levulose and at the end of the second hour it falls to 10 mg per 100 cc. The values above these are indicative of hepatic dysfunction. The test is considered a reliable one and widely used by the British surgeons.

PROTEIN METABOLISM

There are no reliable tests based on protein metabolic function of the liver. Estimations of urea or uric acid are not helpful. *Gelatin Test* has been suggested. 50 g of gelatin are administered and subsequently amino-acids are estimated in the urine. In normal persons 200 mg of amino-acids are present in the first 4 hours, in cases of hepatic disease there is a considerable delay in the excretion and the amount of amino-acids in the early samples is small. The test is not in much use. *Reduction in the serum albumin and reversal of the albumin-globulin ratio* are constantly found in severe hepatic injury. The findings are an index of advanced liver failure but are not a measure of liver function.

FAT METABOLISM

Cholesterol and Cholesterol Esters Cholesterol of the serum is considered a very valuable index of hepatic reserve. The normal value is 200 mg per 100 cc of serum. The amount of cholesterol esters is 100 mg per 100 cc. Changes in the ratio of these two bodies in the blood serum are considered significant. In obstructive jaundice there is an increase in both cholesterol and cholesterol esters, while in acute parenchymatous disease the amount of serum cholesterol is normal or diminished and the esters are diminished or entirely absent. In mild states the initial depression is only moderate and there is a prompt return to normal with clinical improvement. In the differential diagnosis of jaundice the test is useful.

MISCELLANEOUS TESTS

Serum Phosphatase is said to be increased in all forms of liver injury and obstruction. The test is not useful in estimating liver function.

Takata-Ara Reaction This is an empirical test. There is no rationale for its use. Different dilutions of the subject's serum, 1/2 to 1/256 are mixed with 0.25 cc of 10% sodium carbonate and 0.15 cc of 1% solution of bichloride of mercury. The tubes are shaken and the readings taken after 24 hours. The flocculations are graded as 0 Trace 1 2 3, and 4 plus. 4 plus flocculations in two or more tubes are only found in advanced cirrhosis of the liver. Lower flocculations occur in a variety of pathological states. The specific character of the reaction is doubtful. A positive reaction is taken as evidence

of fairly advanced parenchymatous injury. The test is negative in early cases of obstructive jaundice and is useful in the differential diagnosis of jaundice, unexplained ascites, or hepatomegaly. It is not a function test. It is not very sensitive and is not useful in prognosis.

The Cephalin-cholesterol Flocculation Test This is a similar test. 1 cc of cephalin-cholesterol emulsion is added to a centrifuging tube containing 0.2 cc of the patient's serum diluted with 4 cc of normal physiologic solution (0.85 per cent) of sodium chloride. After mixing the contents thoroughly the tube is allowed to stand at room temperature. The readings are made after 24 and 48 hours, and the reactions are graded as 0, trace, and 1 plus to 4 plus. A 4 plus reaction indicates complete flocculation leaving the supernatant fluid quite clear. The test is positive in all cases with acute hepatitis, cirrhosis and chronic passive congestion of the liver, and in cases of carcinoma the reaction seems to be related to the extent of malignant involvement. In obstructive jaundice the reaction is negative or only 1, or 2 plus, and the test may be used to differentiate obstructive from parenchymatous jaundice. The test runs parallel with the clinical improvement. Being very sensitive the reaction is useful in detecting subclinical or mild forms of hepatitis. The test has demonstrated the striking number of persons with unsuspected disease of the liver. The test is a reliable sensitive test of active damage to the liver, possessing prognostic value. Because of its simplicity, the test is advocated as an ideal routine test for active disease of the liver.

Blood plasma prothombin This is depressed in patients with liver disease and under the circumstances the response to vitamin K therapy is inadequate or even absent. The level of the plasma prothrombin and its response to vitamin K is suggested as an index of liver function.

DETOXIFYING FUNCTION

The Quick Hippuric Acid Test To test the detoxifying function of the liver various substances such as thymol, menthol, camphor, salicylates, phenol, and p-cresol, and guaiacol sulphuric acid have been used but without much success. Hippuric acid test is the only one which has met with success. It is a simple, cheap and reliable test. Its findings are entirely compatible

with the clinical findings, other tests of hepatic function, and the pathological state of the liver. The results are always consistent. The test is based on the ability of the liver to conjugate benzoic acid and amino-acetic acid (glycine) to form hippuric acid, the conjugation depending largely on the rate at which the liver can supply glycine. In the presence of normal blood urea, *i.e.*, when the renal function is normal, the hippuric acid excretion after a dose of sodium benzoate, can be correlated with the degree of hepatic injury.

5.9 g of sodium benzoate dissolved in 30 cc of water is given by mouth to a fasting patient. From the same glass he is made to drink about 6 ozs of water. The bladder is emptied and the urine discarded. All the urine voided during the next 4 hours is collected as a single specimen and the amount of hippuric acid in it is estimated.

For the intravenous test 1.77 g of sodium benzoate dissolved in 20 cc of water is used and the amount of urine secreted in one hour after the injection is collected.

The amount of hippuric acid expressed as benzoic acid excreted after the oral test is 3.0 g and after the intravenous test 0.7 g in normal subjects. 85 to 115 per cent of this value is set up as the normal range. The test is valueless in the presence of renal failure.

The hippuric acid test measures the maximum functional capacity of the liver, as it is dependent on the hourly production of glycine and conjugation by the liver with benzoic acid which is supplied in excess of the liver's capacity to conjugate within a fixed period of time.

In studying the hepatic function with hippuric acid test a series of tests repeated at intervals is desirable. The depression of the hepatic function to 50 per cent or under indicates a grave surgical risk. Subclinical or latent hepatic injury can be detected by this test and the improvement after appropriate therapy can be measured.

One may mention in passing that the estimation of blood amylase (diastase), lipase, iodine, sodium-D-lactate tolerance, tyrosine test, cinchophen test, chloral hydrate test are some of the other tests used in the study of hepatic pathology.

CONCLUSIONS

The various laboratory procedures used in the study of disease of the liver give valuable information to the clinician, equally useful in diagnosis, prognosis, and therapeutics.

Some of these procedures should be used more frequently and at least one or two such as the hippuric acid test and the cephaline-cholesterol test should become routine tests for detecting latent disease of the liver.

The bromsulphthalein excretion test, azorubin S test, bilirubin tolerance test, the icteric index, the cephaline-cholesterol flocculation test, and the hippuric acid test are simple, reliable, and fairly sensitive tests of hepatic parenchymatous injury. By their use it is possible to detect cases of latent hepatic injury, or cases of subclinical or mild hepatitis. They are also useful in judging the clinical improvement of the patient under observation.

In cases with jaundice, some help can be obtained in differentiating hepatogenous from obstructive jaundice by the use of van den Bergh reaction, galactose tolerance test, estimation of plasma cholesterol and cholesterol esters, the value of serum phosphate, and the urobilinogen test.

Daily variations in the serum bilirubin give useful information regarding the functional activity of the liver.

Liver function should always be estimated before operations on the biliary tract, cases of hyperthyroidism, all major operations in subjects where there is suspicion of liver damage, intestinal obstruction, and burns. In medical cases all patients with digestive disorders should be subjected to liver function tests together with those who have obvious clinical signs of liver disease. Function tests should also be carried out before and during the use of such hepatotoxic drugs as the arsenicals, mercurials, and the sulphonamides. Serial examination should be the rule rather than a single observation.

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TAKATA-ARA REACTION

A PRELIMINARY REPORT

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N D. PATEL

MD, MRCP, FCPs

I have carried out the Takata-Ara Reaction, with my friend Dr B G Afzulpurkar, 84 times in 60 patients. This admittedly is too small a number to read a paper before you, or to draw any reasonably valid conclusions, especially when it has not been possible for us to follow up the autopsy or to do the biopsy in most cases. My only apology for speaking before you today is to get you interested in the reaction because the results obtained by us so far are sufficiently interesting to induce us to continue our work in a bigger series of cases where damage to the hepatic parenchyma is suspected. My talk this afternoon will be purely clinical, I have no statistical analysis or biochemical data to put before you. Nor do I propose to place a complete historical sketch of the reaction before you. In the literature there are admirable surveys, the latest being that of Magath (1940), who reviews as many as 88 papers on the subject and comments on the "obsession of the medical mind of devising and using a simple and if possible, bedside test to make an absolute and never failing diagnosis in an extremely complicated and involved disease of diverse manifestations, such as the cirrhosis of the liver."

Since 1930, when Jezler modified the technique of the Takata-Ara reaction and used it as a diagnostic measure for cirrhosis of the liver, a vast number of papers have appeared on the subject in America and on the Continent of Europe. But there is little of uniformity of opinion about the usefulness of the test as a diagnostic measure, or about the mechanism of the reaction. On the one hand, the reaction is considered to be a specific one for cirrhosis of the liver (Jezler, 1930), on the other hand its diagnostic value is completely denied, the reaction being found positive in a variety of diverse clinical

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conditions and especially where the serum globulin level is elevated (Kirk, 1934) Bowman and Bray (1937) state that the test was "not significant enough to be of value in the clinic as an additional laboratory procedure" A middle way is adopted by the Mayo Clinic workers who found the reaction to be almost universally positive in the presence of advanced parenchymatous liver injury (Snell, 1936) Snell considers the test to be of considerable value in the study of unexplained ascites, in the detection of the cause of gastro-intestinal bleeding, and in determining the nature of hepatic enlargement

Waugh and McKenna (1942) considered this difference of opinion about the usefulness of the test to be due to lack of uniformity in the technique employed by different workers and also to the difficulty in reading the results of the reaction To avoid this they used a standard technique and a method of reading the result and performed 300 tests on patients who for the most part showed hyperbilirubinemia or gave reason to suspect the presence of hepatic disease They arrived at the conclusion that the test carried out with the method suggested by them has a considerable diagnostic value They state that Takata-Ara reactions with sufficient precipitate to be classified as positive according to their criteria occur almost exclusively in cases of peri-insular cirrhosis of the liver

Takata (1925) used the reaction at first to differentiate broncho from lobar pneumonia Takata and Ara (1925) used the reaction on the cerebro-spinal fluid to differentiate cerebral syphilis from meningitis Perhaps Levinson's Test to differentiate tubercular from pyogenic meningitis is a further application of this principle Jezler (1930) at the suggestion of Staub (1929), used the reaction in cirrhosis of the liver, and obtained 38 positive reactions in 42 cases of cirrhosis He obtained positive reactions also in pseudocirrhosis, yellow atrophy, chronic alcoholism, and passive congestion of the liver Kirk (1934) who reviewed the extensive literature accumulated in the course of five years found that the test was reported in as many as 3,583 cases and was found to be positive, apart from cirrhosis of the liver in a variety of widely different clinical conditions such as abscess, tumour, leukaemia, tuberculosis, nephritis, passive congestion, hyperthyroidism and haemolytic jaundice Of 375 tests on cases of cirrhosis of the liver collected by him

it was reported positive in 315 cases (80%) Magath (1940) collected reports on 1,270 cases of cirrhosis of the liver with positive results in 1,038 cases (82%) Magath found the evaluation of the work of different workers extremely difficult because the technique of the test was not standardised and many different criteria were used for reading a positive reaction. He also found the reported positive reaction in such diverse conditions as stomach ulcers, colitis, pulmonary tuberculosis, nephritis, pellagra, secondary syphilis, mental maladies, lobar pneumonia, and in children with severe typhoid fever or septic conditions, where the colloidal state of the blood serum was changed or the detoxicating function of the liver was disturbed. Magath noted the general opinion about the test in the literature that it is positive where there is advanced damage to the hepatic parenchyma from any cause whatever. Waugh and McKenna (1942) adopted a standard method of performing the test and of reading the result and performed the test 300 times, and found it to be positive 12 times, plus-minus 11 times, and negative 277 times. Of positive 12, all except 1 were proved to have cirrhosis of the liver, of the 11 plus-minus, 3 were Laennec's atrophic cirrhosis, 4 biliary cirrhosis, 1 arsenical hepatitis, 1 lymphosarcoma, 1 extensive pulmonary tuberculosis with involvement of the suprarenals, and 1 multiple myeloma. Of the 277 negative results only 2 were known to have cirrhosis of the liver, one an early periportal cirrhosis and the other a typical atrophic cirrhosis proved at the autopsy.

THE METHOD

The technique of the Takata-Ara reaction is said to be simple. But from the perusal of the literature it does not appear to be so. Otherwise one does not see why as many as 14 different modifications have been suggested by different workers (Takata-Ara, Jezler, Heath, Uko, Crane, Hofstom, Mancke and Sommer, Wayburn and Cherry, Magath). Noting that the discrepancy regarding the evaluation of the Takata-Ara reaction was apparently due to the differences in the methods employed in carrying out the test and in reading and interpreting the result, Waugh and McKenna have suggested a standardised technique and a fixed method of reading the result. We have followed it in our work and it is reproduced below in full detail from their article.

¹ The test may be done on blood serum, plasma or transudates such as ascitic fluid. Most of our results were obtained from oxalated plasma procured at the time of carrying out a complete hemogram. Blood is usually taken for such tests in the morning between 10 and 12 O'clock to avoid any effect of digestive processes on the plasma. At least 1 c.c. free from hemolysis and cells is required.

² A series of 8 tubes approximately 10 cm. in length and inner bore of 1 cm. are placed in a rack. The tubes must of course be thoroughly cleaned. One cubic centimeter of 0.9% NaCl is pipetted into each tube and 1 c.c. of plasma added to the first tube. This is mixed with the saline by shaking and 1 c.c. of the mixture withdrawn and placed in the second tube. By continuing in this manner and drawing 1 c.c. from the last tube a series of increasing dilutions (1 to 1/256) of plasma in saline is set up. To each tube first 0.25 c.c. of a 10% solution of sodium carbonate and then 0.15 c.c. of 0.5% biichloride of mercury are added. Complete mixing is obtained by shaking after each solution has been placed in the tube. A slight precipitate which disappears on shaking may occur after addition of the mercury reagent. The series of tubes is then allowed to stand at room temperature for 24 hours.

At the end of this interval the result of the test is read by estimating the amount of precipitate in each tube. This is expressed as O.T. (Trace) 1, 2, 3, or 4. Precipitates classed as 4 occupy approximately the lower third of the solution in the tube. In doubtful cases accurate reading of the amount of the precipitates may be accomplished by thoroughly shaking up the tube and filling Wintrobe sedimentation tube to the 10 cm. mark with a portion of the contents. The Wintrobe tube is then centrifuged at high speed for 15 minutes. Less than 1 mm. of whitish sediment in the bottom of the tube is classed a trace. T 1 to 2 mm. as 1, 2 to 3 mm. as 2, 3 to 4 mm. as 3, and amount over 4 mm. is designated 4.

The Takata Ara reaction is positive when two adjacent tubes show a Grade 4 degree of precipitate and the next tube is at least a Grade 3 for example (00T21441) or (00134421). Plus minus reactions are reported whenever the criteria for the positive reaction are not reached but at least two tubes show a Grade 3 sediment for example (00T12431) (0001331) or (0001T332). All reactions of lower degree are negative as (000T231) or (0000T1TT). It would appear from an analysis of our findings that accurate reading of the reaction is extremely important.

The flocculation or characteristic precipitate is a white to pearl gray, large flaked flocculent. The appearance of a fine brick red precipitate is of no significance.

THE MECHANISM OF THE REACTION

Takata considered the reaction to be a result of the albumin-globulin shift in cases of lobar pneumonia. Staub expecting such a shift in cases of cirrhosis of the liver suggested the test to Jezler who believed that the reaction was produced as a result of relative increase in the amount of the serum globulin. Mercuric chloride and sodium carbonate form mercuric oxide in the presence of proteins which are considered to act as protective colloids. In certain pathologic states precipitation of the colloid occurs because the albumin-globulin ratio in the serum is altered.

Disturbance in the albumin-globulin ratio, lowering of the protein level, increase in the globulin fraction, adsorption of the mercuric chloride by the protein, some new metabolite produced by the damaged liver increased fibrinogen, presence of acidosis, faulty sulphur metabolism which removes the protective sulphuric compound from the globulin, release of the liver proteins in the circulation, inability of the liver to alter proteins contained in the blood, failure of some blood to pass through the liver—all these hypotheses have been suggested as the cause of the precipitation by the alkaline sublimate solution and objections have been raised against each one of them.

Wayburn and Cherry (1938) agree with Jezler that "the Takata-Ara reaction represents a liver dysfunction. It pro-

bably represents some retentive substance which under the usual conditions of its occurrence requires some time to be formed in sufficient quantity to result in a positive reaction," (cf blood urea in nephritis)

Magath (1940) concludes after a lengthy review of the subject that "The reaction is likely to be due to a more fundamental change in the body fluids, which often, perhaps more often, is due to dysfunction of the liver than to that of any other organ but which may be caused by the dysfunction of the other organs, and results in colloidal changes in various bodily fluids, such as serum, spinal fluid, and fluids secreted by serous surfaces"

ANALYSIS OF RESULTS

Of the 84 tests performed 14 were positive, 14 were plus-minus and 56 were negative 57 tests were done on blood serum, 25 on ascitic fluid, and 2 on pleural fluid The total number of patients examined was 60 The clinical diagnosis and the results are given in the following table

TABLE
TAKATA-ARA REACTION IN DIFFERENT CLINICAL CONDITIONS

Clinical Diagnosis	Number of patients	Number of tests	Positive	Plus minus	Negative
Cirrhosis of the liver	10	21	8	7	6
Infantile Cirrhosis	1	1	1		
Amoebic Hepatic abscess	9	12	2	6	4
Jaundice	6	6			6
Anasarca Ascites	7	11			11
Tubercular Peritonitis	4	6			6
Hepato splenomegaly	5	5		1	4
Pleural Effusion	1	1			1
Congestive Cardiac Failure	7	8			8
Nephritis with Anasarca	6	6			6
Aggranulocytosis	1	1			1
TOTAL	60	84	14	14	56

Of the 60 patients examined 10 had cirrhosis of the liver Of these 8 tests were positive, 7 plus-minus and 6 negative These latter were tests on the ascitic fluid We have noted that the reaction in the ascitic fluid is often plus-minus or negative even when the reaction in the serum is fully positive Sometimes the reaction which was plus-minus or negative at the first examination became fully positive at the second examination This suggests that the biochemical factor responsible for the Takata-Ara reaction is not present in the ascitic

fluid when it may be present in the blood serum. Here also it may be present only intermittently and not constantly. In all cases of cirrhosis of the liver both atrophic and infantile hypertrophic types, the reaction was positive. The reaction was not positive in any other condition except in two cases of amoebic abscess. One of these cases was a very big abscess of the liver which had ruptured into the pleura and the patient came in a cachectic state with ascites and anasarca. The post-mortem showed that the whole of the right lobe was occupied by the abscess and there was very little liver tissue left. It is also interesting that one other case of liver abscess gave positive reaction and as many as six tests were plus-minus in cases of liver abscess. This suggests a diffuse parenchymatous damage to the liver cells or production of some metabolite by the autolysing liver cells. It will be interesting to follow up these cases of liver abscess with positive or plus-minus results who make a clinical recovery to find out when the reaction disappears from the blood, if at all. All 6 cases of obstructive jaundice gave a negative result. One of these patients at the operation showed a very early type of obstructive cirrhosis, confirmed by the histological examination. This shows that the reaction may not be positive in early cases of obstructive cirrhosis. Only one other case where the reaction was plus-minus was a case of primary hepatoma (? malignant) with a polycystic right kidney.

CONCLUSIONS

The Takata-Ara reaction performed and read as described above is a test of high diagnostic value in cases of advanced cirrhosis of the liver. A positive reaction implies cirrhosis of the liver or marked diffuse parenchymatous hepatic damage. A plus-minus result has also a similar importance. But it is not a specific test.

It is not a very sensitive test and is only positive when the pathological state is fairly advanced.

It is an empirical test and there is no agreement about its mechanism. It is correlated with changes in the serum albumin-globulin ratio and especially with the increase in the beta or euglobulin of the serum.

The test when positive shows an advanced degree of hepatic damage and to that extent it has a prognostic and therapeutic

value In its presence, all drugs, likely to damage liver cells, should be withheld and measures should be adopted to protect and help the regeneration of the liver cells

It is not a test of liver function

It is a pleasure to thank Dr B G Afzulpurkar Pathologist to the P G S Hindu Hospital, who collaborated with me and Dr R Row, M D D Sc, (Lond), Director of the P G S H Hospital who gave us all the facilities to do the work there

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DISCUSSION

Dr R G Ginde mentioned a case referred to Dr Cooper's surgical unit for diagnosis The patient an elderly man had ascites, enlarged liver and deep jaundice Because of the deep progressive nature of the jaundice, secondary carcinomatosis of the liver was suspected But in this case, the Takata-Ara test was negative The barium meal of the gastro-intestinal tract revealed no abnormality Exploration of the abdomen showed that the liver was markedly enlarged and finely granular The stomach was normal There was lot of free fluid inside which was sucked out A wedge from the left lobe of the liver was excised and sent for biopsy which showed early cirrhosis of the liver

Dr V N Patwardhan suggested that strongly positive Takata-Ara reaction in absence of a change in albumin-globulin ratio could be explained by assuming that the nature of some component of the globulin fraction had altered That such changes occur can be demonstrated by electrophoretic methods and it would be worth while submitting the serums of cirrhotic cases to such tests

Dr R G Dhayagude while summing up the discussion of Takata-Ara test remarked that he owed his interest in this test to Dr N D Patel who suggested that it might be tried in this Hospital The reports in the literature as regards the value of this test have been conflicting and that might be due to the fact that the technique adopted by different workers varied considerably Unless a standard method was used the results were not comparable One of his colleagues Dr P D Khanolkar read a paper in the Society of Teaching Pathologists on this test and he had come to the same conclusion as Dr Patel that the test was not a very sensitive one and was only useful from the point of view of confirmation of the diagnosis of cirrhosis Other diseases in which there was a disturbance in the fractions of the globulins of the blood gave positive results and must be excluded He complimented Dr Patel for his efforts to correlate the laboratory findings with the clinical data

THE QUICK HIPPURIC ACID TEST FOR LIVER FUNCTION

A PRELIMINARY REPORT

By

P RAGHAVAN

M D (BOM)

The liver has many functions to perform and there has been a tendency to attribute to the liver all those metabolic and detoxifying functions, which cannot be proved to take place elsewhere. However to list only those functions which are fully established, is to mention the following

- 1 Metabolic Carbohydrate—storehouse of glycogen, Conversion of laevulose and galactose to glycogen
 Proteins—Deamination of proteins—conversion into urea
 Bile—Synthesis of bile acids excretion of bile pigments
- 2 Coagulation of blood—formation of fibrinogen formation of prothrombin
- 3 Detoxification—of chemicals, bacterial toxins, and noxious metabolic products
- 4 Thermogenic action

This multiplicity of functions and the capacity to carry on these functions normally far in excess of physiological needs, even when four-fifths of the total liver tissue is destroyed (either by experimental ablation or by disease), make all the liver function tests devised so far, open to certain objections. As no single test takes into consideration all the functions, it gives us information about that particular function on which it is based at a time when the liver is already extensively damaged. It has been said that all the existing function tests give us information at a time when we do not need it, in other words when clinical manifestations of hepatic deficiency are already in evidence. These objections are true of all the tests and cannot be argued against a particular one.

The common tests employed today are the icteric index, van den Bergh's test, Bilirubin test of Von Bergman and Elliot and the laevulose tolerance test, and other tests which use the excretion of a foreign substance like tetrachlorophenolphthalein, camphor, etc. Mann laid down years ago that any substance that is used should be such that all or a major part of it should be excreted by the liver and the product should be capable of quantitative measurement directly or indirectly.

Among the simpler tests the icteric index and van den Bergh's test tell us about jaundice and are useful to distinguish

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haemolytic from obstructive jaundice in its early stages. The laevulose tolerance test necessitates multiple venepunctures and is expensive. Besides this the substance can be utilised by the muscles also as experiments of Mann and Bollman (1931) demonstrated that hepatectomised animals can still utilise levulose. The dye test is expensive and needs multiple radiograms. About the Takata-Ara test and its value D. N. D. Patel has already spoken and I shall not go into its details.

In the search for a simple test, that does not involve much of expense, multiple venepunctures or necessitate the use of elaborate equipment, the Quick hippuric acid test strikes one as free from the many disadvantages of the other tests while it has advantages of its own. As late as 1925 the excretion of hippuric acid was used as a measure of renal function. The evolution of this test as one for liver function is largely due to the work of Quick and is certainly interesting.

Hippuric acid was first synthesised by Wohler in 1824. Bunge and Schmeidberg in 1877 perfused kidneys of dogs with benzoic acid and amino-acetic acid, and recovered hippuric acid. Confirmation of this work came from Kochs in 1879 and Cramer in 1902. On the other hand Kuhne and Hallwachs expressed in 1857 the view that synthesis might occur in the hepatic vessels in the presence of glycocholic acid. Friedman in 1911 isolated hippuric acid after perfusing the liver of rabbits with blood containing benzoic acid but no glycine and concluded that in the rabbit at least the synthesis occurs in the liver.

Kingsbury and Bell in 1915 found hippuric acid in the liver of nephrectomised dogs after injection of benzoic acid and glycine, and suggested that apparently the kidneys are not the only organs where synthesis of hippuric acid occurs. Lackner, Levinson and Moise, in 1918 poisoned dogs with hydrazine sulphate which is known to affect only the liver and found that synthesis of hippuric acid was greatly diminished. Delprat and Whipple in 1921 showed that when the liver is damaged by chloroform the synthesis of hippuric acid is greatly diminished. In 1925 Bryan who was using the test for renal function as was the vogue at that time, found that in 6 out of 10 cases where hepatic involvement was known to be present, there was definite fall in the quantity of hippuric acid excreted. Though he advanced the view at that time, that low values may be due to hepatic damage, it was not until 1932 when Quick published his

results and suggested that the test may be used as a measure of hepatic function

While studying the conjugation of benzoic acid in man, Quick found that the excretion of hippuric acid proceeded at a uniform rate depending upon the surface area of the individual, irrespective of the amount of sodium benzoate administered and that the rate could be increased by ingestion of amino-acetic acid or food rich in it. It was clear that the rate of synthesis of hippuric acid depended upon the rate at which the body could mobilise amino-acetic acid. Since it is known that the liver is the main site of synthesis of amino-acetic acid, Quick reasoned that the conditions of hepatic damage, the excretion of hippuric acid might show a diminution, and the test which upto that time was used as a test of renal function should actually be a more delicate test of liver function. His further work and the work of later workers has fully justified the hopes and has demonstrated the value and clinical applications of the test.

Certain of the possible objections were anticipated and answered by Quick himself. It may be contended that the test will give information of value in conditions of extreme hepatic damage, since the reserve power of the liver is enormous. Quick pointed out that the function of synthesis of amino-acetic acid seems to have a great margin of reserve. There is no preformed store of amino-acetic acid in the body and the synthesis proceeds at uniform hourly rate which depends upon the surface area of the individual. As such, the test is likely to convey information earlier than other tests. To the objection that it gives information about the particular function only, he pointed out that the synthesis of amino-acetic acid depends upon certain intermediary products of carbohydrate metabolism and is closely related to other process like synthesis of bile acids. It is one link in a chain of processes. Besides these, the test is simple and inexpensive. The oral test does not necessitate venepunctures at all. The intravenous modification which was introduced by Quick later, needs only one venepuncture and takes only one hour to perform.

The technique of the test is as follows. The subject is started after his dinner overnight. At 5 a.m. of the day of the test, he is given a plain toast and a cup of tea after which he is given or allowed no food, water or drink till the test is over. At 6 a.m. he is given 5.9 grams of sodium benzoate (equivalent to 5 grams of benzoic acid) dissolved in half an ounce of water. In the same glass in which the powder has been given he is given another half a glass of water to drink washing down all the powder. Immediately afterwards he voids his bladder and the specimen is discarded. From now on till 10 a.m. all the urine he passes is collected in a receptacle and preserved. At 10 a.m. he empties his bladder again and all the urine that is passed is collected. If he cannot empty his bladder by himself he is catheterised and bladder is emptied of its contents which are collected. After acidification with glacial acetic acid the volume of the sample of urine is concentrated by boiling to

about 150 c.c. After cooling, the hippuric acid is precipitated by addition of concentrated hydrochloric acid till it turns congo red solution blue, combined with vigorous stirring. The specimen is left in the refrigerator for 24 hours after which period it is filtered through a weighed filter paper over a buchner funnel. The volume of the filtrate is noted and the precipitate along with the filter paper is transferred to a small beaker of known weight and dried in vacuum. After drying, beaker and the contents are weighed from which the weight of the precipitate is calculated. The weight of hippuric acid in solution in the filtrate is calculated by multiplying the volume of filtrate in c.c. by 0.0013. This is added on to the weight of precipitate and the sum gives us the total weight of hippuric acid excreted. It is best to express the results in terms of benzoic acid and this is obtained by multiplying the total weight of hippuric acid excreted by 0.68. In the normal subject the result is over 1 gm. Values under this are indicative of parenchymatous hepatic damage.

Quick later on introduced an intravenous modification of the test in which 1 hour after the preliminary toast and tea he injects 1.77 grams of sodium benzoate in 10 per cent. solution intravenously and collects the specimen of urine 1 hour later. The hippuric acid excreted is estimated by the same method as above. Result below 0.7 gm. is expressive of hepatic damage.

One of the practical considerations in the interpretation of the test is, where renal function is deficient, hippuric acid like all other nitrogenous products will be retained and the test must be interpreted accordingly. Another consideration is dehydration. Snell has suggested that there is some relation between the excretion of water and hippuric acid and erroneously low values are likely to be obtained in dehydrated subjects. Again, in states of inanition where the liver is likely to be depleted of its glycogen reserves, low values may be obtained. In the presence of the conditions mentioned above the test must be interpreted with caution.

Though a single test gives us some information, repeated tests (particularly when the result shows either a decrease or increase) are more valuable. It is of interest to the surgeon, as a low value indicates a stormy post-operative course with possible fatal result due to hepato-renal failure as has been shown by Kohlestadt and Helmer, Yardumian and Rosenthal and Boyce and MacfetrIDGE. The possibilities of the test with a view to avoid 'hepato-renal' deaths was studied by Boyce and MacfetrIDGE and they have suggested that where a low pre-operative value is found, adequate preparation of the patient with dextrose and fluids is indicated before he is subjected to the operation.

The test is also of value to differentiate intra-hepatic from extra-hepatic jaundice, when the condition is of short duration. In intra-hepatic jaundice low value is obtained whereas in extra-hepatic jaundice normal value is obtained. If the condition is of some standing there is sufficient parenchymatous damage produced and differentiation on the basis of this test becomes impossible.

To date I have done the test on 10 normal subjects (medical students and physicians) eight of them showed values over 3, the highest being 4.09, two of them showed values below 3, lowest

being 2.5 I have also done the test in a number of patients with diseased states and the results are summarised below

TABLE

Pathological condition	No. of Cases	Range of values in gms
Cirrhosis of Liver	3	1.54 to 0.83
Catarrhal Jaundice	4	1.58 to 1.31
Obstructive Jaundice	1	1.17
Amoebic abscess of liver ruptured into lung	1	3.01
Banti's disease (Splenic anaemia)	1	7.64
Secondary Syphilis	4	7.5 to 1.66
Cystitis	1	3.5
Anaemia	5	5.0 to 1.02
Spinal tumour with anaemia	1	1.45
Malaria	2	2.83 to 2.38

I propose to continue the work particularly in cases of cirrhosis of liver, catarrhal jaundice and amoebic abscess of liver. I shall communicate the results to you later. Two patients were followed up, and were interesting as their histories cited below will show.

One of the cases, who was admitted for progressively deepening jaundice of a month's duration had a hard lobulated lump in the right hypochondrium. The first time I did the test I could not get any precipitate even after concentrating the volume to 100 cc. Two weeks later he showed a result of 1.43. He was given glucose by mouth and insulin subcutaneously and after two weeks of such treatment showed a result of 2.06. By this time the jaundice diminished in intensity and the lump in the hypochondrium receded gradually. His gall-bladder was drained daily by Lyon's method and the jaundice disappeared completely but he left the hospital before we could repeat the test.

Another patient with cirrhosis of liver and ascites showed a value of 1.54. He was given $\frac{1}{2}$ cc of Neptal intraperitoneally. He had a marked diuresis but became semicomatose. He recovered after 2 days with administration of intravenous dextrose. The fluid reaccumulated in the peritoneal cavity and he was again given neptal after a week. He went into a semicomatose condition, but recovered this time also with administration of intravenous dextrose. He was given dextrose solution intravenously with insulin daily for two weeks. At the end of this period the result of the test showed a value of 2.25. He was handed over to the Surgeon for splenectomy. On opening the abdomen his liver was found to be cirrhotic. The spleen was removed, but the haemorrhage from hilar vessels could not be controlled and he died.

As the test is simple and is of value both to the surgeon and the physician it is hoped that it will be used by both more often than at present

It is a pleasure to express my thanks to Professors S P Neogi and V N Patwardhan, Dr N D Patel and the late Dr J P Padshah, and the medical registrar and house man of the unit

DISCUSSION

Dr R N Cooper stressed the importance of hippuric acid test in thyroid surgery. He also indicated that the test may be of value in determining the changes attending sulfanilamide therapy.

Dr N D. Patel said that Boyce's publications on the practical utility of the Quick's Hippuric Acid Test for estimating liver function aroused his interest and he suggested the use of the test in the wards. Dr Raghavan kindly undertook to do the test and the results appeared to be a great promise. The test is of definite clinical value and he proposed to continue using it in all cases of jaundice, supposed liver damage in arsenical or other poisoning, sulphanilamide poisoning, Graves' disease, etc. The surgeons and obstetric physicians should also use this test in case of pregnancy toxæmia and before operations especially in cases of gall-bladder disease, acute abdomen of upper abdominal pathology and hyperthyroidism. Boyce has shown that acute liver deaths (occurring within 24-48 hours, or in 4 or 5 to 10 days) all were due to a hepato-renal syndrome, the possibility of which could be diagnosed before operation and the patient can be prepared by adequate pre-operative treatment. He has shown the danger of operating in cases where the hippuric acid estimation was under 50% and which could not be raised by appropriate therapy. His conception of liver deaths or hepato-renal syndrome due to a pre-existing hepatic damage made fatal by effects of anaesthetic and surgery is backed up by clinical and experimental evidence.

Dr R G Ginde said that the amount of glycogen in the liver, affects the results of the test and therefore it would be better if all patients on whom these tests are done are given a known quantity of glucose either by mouth or by injection before this test is done to have uniform results.

Dr. V. N. Patwardhan did not agree with the author's statement that the muscles could utilise laevulose. Experiments on hepatectomized animals showed otherwise. He also pointed out that hippuric acid formation might give an idea of the state of that particular function of the liver but not necessarily that of the others. He suggested that a number of tests purporting to indicate the efficiency of liver in one way or other should be tried by a team of workers on several cases and at the end attempts should be made to find one test which would give most information in condition involving the liver.

Dr R G Dhayagude congratulated Dr Raghavan and Dr Patel on their undertaking a problem in clinical research and he hoped that they would very soon be able to give an idea of the values of excretion of hippuric acid in normal persons. Liver function tests have always been an interesting problem and none of the tests so far devised give a correct idea of the amount of healthy liver parenchyma. That was to be expected as the organ had more than a dozen functions to its credit and a test which assessed one function, neglected the other. Hippuric acid excretion was a good index of its detoxifying function and the clinical correlation of this test had yet to be worked out.

RECENT ADVANCES IN THERAPEUTICS

AS INDICATED BY THE TWELFTH 1942 EDITION OF THE
UNITED STATES PHARMACOPOEIA

By

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(Continued from p 233)

DIURETICS

Certain xanthine derivatives and their preparations have been added to the new USP *Theophylline*, which was already added to the BP by the first addendum (1936) is included in the USP in the form of tablets and two other preparations, viz, *Theophylline with Sod Acetate* (already in the BP) and *Theophylline with Ethylenediamine* (aminophylline or euphylline), both as tablets and injections. The Ethylenediamine accelerates the effects of theophylline by making it more soluble. *Theobromine with sodium salicylate* has now been deleted and its place is taken by *Theobromine with Sodium Acetate* because the latter is considered better and because it "eliminates the chance of harm to diseased kidneys from the salicylate radicle". All these xanthines possess the same type of action but there is the belief that some patients tolerate one derivative or preparation better than another.

Urea (already in the BP) is another diuretic newly added to the USP for oral administration, as an alternative to the xanthines, especially when the latter cause side actions due to central stimulation or local irritation. It is probably the best "saline" diuretic when the blood urea is normal. Some oedematous patients, however, especially those with chronic nephritis, do not react to the foregoing diuretics and potassium salts are sometimes of great benefit in such cases. Potassium salts, after absorption, are present in the extracellular fluid, are filtered out through the glomeruli and rejected by the tubules. They carry water with them and also lead to the excretion of sodium. They are effective in any concentration. When the potassium action is desired, the two salts which are most commonly employed are potassium nitrate and potassium chloride. Potassium nitrate (both the ions) and urea are non-threshold bodies and so potassium nitrate (already in the BP and previous USP) produces a greater diuretic effect than any of the other salts of potassium but according to some authors it is apt to cause irritation of the kidneys. So *Potassium chloride*, the salt next to it in efficiency, has now been added to the USP as such and also as tablets.

Potassium is often more effective when combined with a diet low in sodium chloride. Potassium chloride rather than sodium chloride may then be used to flavour the food.

The organic mercurials are useful for those cases in which oral diuretics and xanthine derivatives do not suffice. They have the justified reputation of being the most powerful and consistently effective of all diuretic drugs, and they produce diuresis even in normal individuals. Merbaphen (novasurol) was the one organic mercurial previously included in the USP but it is deleted because its use is now largely abandoned in favour of the less toxic and more effective Mersalyl (salyrgan) which is now admitted both to the BP (1st addendum) and to the new USP as *Mersalyl and theophylline injection* (in ampules containing a dose of the 10% solution of mersalyl with theophylline). *Injectio mersalyli* (BP) is also a 10% solution of mersalyl with 5% theophylline, although the name does not indicate its presence, the theophylline being added to prevent the decomposition of mersalyl in solution, the products of which are toxic. Another organic mercurial injection now added to the USP is the *Mercurphylline injection*, a solution of mercupurin, a combination of mercurin and theophylline, the two molecules being probably chemically combined. *Mercurin*, one constituent of mercupurin has also been added to the USP as such but it is an insoluble powder and so unsuitable for injection. It is used in suppositories by the rectal route. A noteworthy feature of both the new mercurial injections, in contrast to merbaphen in the previous edition, is that the mercurials are in combination with a xanthine (theophylline). In this, the new USP has taken account of the recent evidence indicating that the addition of a xanthine to an organic mercurial reduces the local irritant action and toxicity of the latter. It is doubtful whether the xanthine adds significantly to the diuretic action of mercury, but it may increase the rate of absorption of the mercurial from the tissues. The effect of the mercurials is, on the other hand, enhanced if a mild acidosis is produced by the administration of ammonium chloride a day or two before the injection of the mercurial. Experience seems to favour the intramuscular route, although the intravenous route is sometimes preferred. On intravenous injection, sloughs and venous thromboses occur with less frequency with mercupurine than with mersalyl. Otherwise, the present indications suggest that mercupurin is on a par with mersalyl with respect to diuretic activity and toxicity. Two mercurials have been admitted to the new USP because there may be patients hypersensitive to one but show no intolerance to another.

THE GENITAL SYSTEM

Of the alkaloids or ergot, ergotoxine ethanosulfonate was already included in the previous USP and it has a place also in the BP, but it is seldom employed therapeutically in the USA. It has been used only in animal experiments and as a reference standard for the ergot preparations. Now, two other ergot alkaloids have been added

to the USP *Ergotamine tartrate* (gynergen) and *Ergonovine* (ergometrine—BP, or ergobasin, ergotocine, ergostertrine) malate, each in two forms, viz, tablets for oral and sublingual administration and injection in ampules. Both ergotoxine and ergotamine have similar pharmacological actions, qualitatively and quantitatively, but the latter is used therapeutically in the USA for its action on the uterus as well as for autonomic (sympathetic) blocking. *Ergonovine* is a water-soluble alkaloid recently isolated. The activity of the (old) watery extract of ergot was due to its presence. It shares with the aforementioned alkaloids the property of causing uterine stimulation but is more readily absorbed and the onset of its action is rapid. It is not sympatholytic while it appears to stimulate certain organs in a manner similar to the sympathomimetic drugs.

A dangerously toxic drug *Veratrum viride* and its tincture which are little used now but which were sometimes recommended in large doses in eclampsia have been deleted, because reports about the value of the drug are not favourable.

HORMONES

A number of hormonal substances or preparations are now employed in the treatment of the disturbances in the genital functions. Some of their uses have a physiological basis while others are empirical or even have a doubtful value. *Progesterone*, a crystalline substance representing the activity of the corpus luteum has now been added to the BPC (third supplement) and the substance itself and an injection of it have now been taken up in the new USP. It is most valuable in the treatment of habitual abortion and also in threatened abortion. Its function is to maintain proper type of endometrium (including its blood supply) and inhibit uterine motility. The former action can be used in the cases of sterility, thought to be due to failure of nidation and the latter can relieve afterpains and dysmenorrhoea. It is reported to arrest excessive hemorrhage in cases of menorrhagia and it has also been used, in conjunction with oestrogenic substances, in amenorrhoea. But there are many factors involved in the causation of amenorrhoeas and dysmenorrhoeas and the treatment must differ according to the cause. Two oestrogenic substances have now been added to the USP—*Estrone*, as tablets and as injection (in oil) and *Estradiol benzoate* (Progyon). Most satisfactory response is obtained to their use for the relief of the menopausal syndromes and in the climacteric disorders. They are also used in some dermatological disturbances in elderly women. Favourable results have also been reported in acne vulgaris but further study as to their value must be awaited. They are used with success in the treatment of gonorrhoeal vulvovaginitis in children. In these cases they act by changing the vaginal mucous membrane to the adult type. Similar change is also the basis of their use (usually local as suppository) in senile vaginitis. Since the development and growth of the uterus is under the influence of the ovarian hormones, these preparations are useful in the treatment of

uterine hypoplasia. Favourable results are reported from their use in certain cases of frigidity but there is little evidence in favour of their use in sterility. Instead of these ovarian (follicular) preparations, the synthetic oestrogen stilbestrol, which has the same therapeutic indications, has been included in the BPC. It is relatively highly active orally and on injection it is more active than esterone. Estradiol also is more active than esterone and its benzoic ester which gives a much more prolonged action is commonly used for parenteral therapy. Stilbestrol is much cheaper than the natural preparations but its side actions must be weighed against its cheapness, its greater activity on oral use, etc. It has been stated above that there can be a variety of causes for dysmenorrhoeas, amenorrhoeas etc. and that the treatment should be according to cause. Even androgenic substances or male hormone preparations are found to be effective in controlling excessive hemorrhages in certain menorrhagias and dysmenorrhoeas. Experience of the use of the male hormones is yet limited. But there are encouraging reports of more or less improvement and alleviation of symptoms and signs in male castrates and eunuchoidism after the replacement therapy with these substances. Hence, *Testosterone* and *Testosterone propionate* have been added to the BPC (3rd suppl.) and to the new USP in the form of tablets and an injection (in oil). The esters of testosterone have been found to be more potent than the natural product, the propionic ester being the most active. Its use is also advocated for male impotence. It may be of limited value in cryptorchidism. There is incomplete evidence of its value in prostatic hypertrophy. In the females, it often allays symptoms of mastodynia and chronic mastitis, the benefit being also associated with structural improvement. More evidence is necessary for its use in peripheral vascular disease, to produce interruption of lactation, etc.

There is a marked similarity in the chemical structure of the *adrenal cortical* and sex hormones, especially the androgens. Numerous chemically-related compounds are obtainable from the adrenal cortex. Corticosterone and desoxycorticosterone are two of them, desoxycorticosterone being the most potent. But the question whether a single substance can correct the various physiological deficiencies in an adrenalectomised animal or in Addison's disease cannot be definitely answered, because no one compound is found to produce all the effects of the active extracts which have now been introduced into clinical practice under the name of "Cortm". Such extracts called "*Suprarenal Cortex Extract* and *Suprarenal Cortex Injection*" have now been added to the USP. These extracts have proved effective in alleviating the symptoms and greatly prolonging the life in Addison's disease but their great disadvantage is their high cost. Desoxycorticosterone is not the active principle of the cortex because certain fractions obtained from the cortex are 100 times more active. But it appears to be essential for normal metabolism and it is also capable of maintaining life but patients on desoxycorticosterone, if given supplemental extract, show further improvement. Its esterifi-

cation increases its potency and duration of action. Thus its acetic ester, *Desoxycorticosterone Acetate* has now been added to the USP and also to the BPC. In Addison's disease, reduction of potassium intake coupled with high sodium chloride intake i.e. about 10-20 G daily in addition to the normal intake, produces a striking benefit and this is supplemented by treatment with the extract or desoxycorticosterone acetate. The effects produced by suprarenalectomy show a great resemblance to those observed in shock and so cortical extract or desoxycorticosterone has been recommended for the prevention and treatment of surgical shock and good results are reported, although theoretical considerations do not support their use. Before leaving the adrenal gland, it may be added here that a *strong solution* (1 in 100) of *epinephrine* (adrenaline) has been added to the new USP.

Until recently the manufacture of insulin was under the control of the Canadian owners of the patent and it was included in the BP of 1932. In order to protect the public and to prevent its careless unscrupulous manufacture and import it was added to the previous USP by the interim supplement issued before the expiry of the patent. Now the new USP includes *Insulin injection* and the two "slow" insulins, viz, *Insulin Crystalline Zinc injection* and *Insulin Protamine Zinc injection*. The slow insulins have not yet been added to the BP.

VITAMINS

Vitamin research in recent years has made great strides. The markets are now flooded with all sorts of commercial vitamin preparations sold under various names and claims, creating a state of confusion. The discovery of most of the more recent vitamin compounds is the outcome of the researches on the growth and metabolism of experimental animals and not of the study of any human deficiency diseases. Little is, therefore, known about the part they play in human disorders or nutrition. The inclusion of certain vitamins or vitamin preparations in the pharmacopeia is, therefore, an authoritative expression of their therapeutic value and a guarantee for their purity and potency. The new USP now describes suitable preparations of all the vitamins of established value with their average dosage, methods of assay etc. It may be stated, however, that the doses in the USP are prophylactic and larger doses are usually necessary to treat established deficiency diseases.

For the treatment of vitamin A deficiencies (night blindness, xerophthalmia, follicular keratosis) the new USP provides a rich source of vitamin A in *Oleovitamin A*, which corresponds to the *Liquor vitamin A concentratus* in the second addendum to the BP. It is a concentrated solution in oil of natural vitamin A obtained from fresh liver and is required to contain at least 50,000 units of vitamin A per Gram, and not more than 1000 units of vitamin D. Two teaspoonfuls of cod-liver-oil are necessary to supply the amount of vitamin A contained in about five drops of this preparation. It is to be noted that for

vitamin A therapy the pharmacopoeia does not provide any preparations of carotene (the precursor of vitamin A) or synthetic materials for vitamin A. Carotene is absorbed less readily than vitamin A and is subject to several more hazards than vitamin A.

For the prevention and treatment of rickets and other vitamin D deficiencies, the new USP contains a concentrated source of vitamin D in Synthetic *Oleovitamin D*, which corresponds to the *Liquor vitamin D concentratus* of the Second addendum to the BP (a much stronger preparation than *liquor calciferolis* in the 1st addendum) and it is required that the label should state whether the preparation contains vitamin D₂ (activated ergosterol i.e. from vegetable sources like activated ergosterol in oil in the previous USP) or vitamin D (from animal sources) because these two forms of vitamin, D₂ and D₃, have different relative potencies in different species of animals (for example, in the chick a rat unit of vitamin D₃ is nearly 20 times as effective as that of vitamin D₂), and there is some doubt as to the identity of their action in man, although the evidence indicates that their behaviour in man parallels fairly closely their behaviour in rat. The new synthetic oleovitamin D has the advantage over cod liver oil, for the prophylaxis and treatment of rickets, that it is highly concentrated, odourless and has a bland taste. It has the further advantage that large doses of vitamin D can be administered in this form without any vitamin A. It contains 10,000 units of vitamin D per Gram.

Cod liver oil is useful for the treatment of mixed fat soluble vitamin A and D deficiencies and in the previous edition it was the only preparation available for the administration of both the vitamins, but the new USP contains two additional preparations for the purpose, viz *Oleovitamin A and D*, and *concentrated Oleovitamin A and D*, corresponding respectively to *Oleum Vitaminatum* (BP) and *Liq vitaminorum A et D concentratus* (of the 2nd addendum to BP). The former is meant as a substitute for cod liver oil which is now scarce and the latter, especially the concentrate added to the BP, may be considered as a substitute for *Oleum Hippoglossi* (or halibut liver oil) in the 2nd addendum to BP now added to the USP and which, like many Indian fish liver oils, is particularly rich in vitamin A, but contains a variable amount of vitamin D. The vitamin A in the *Oleovitamin* of the new USP is from natural fish liver sources and the vitamin D content may be either from synthetic or natural sources. The dosage of *Oleovitamin* is the same as for cod liver oil, 2 teaspoonfuls representing approximately 700 units of vitamin D and 7000 units of vitamin A. But its potency is likely to be more uniform than that of cod liver oil, because while the pharmacopoeia fixes its potency, it specifies only a minimum potency for cod liver oil. There remains to be considered, however, the possibility that there may be factors of therapeutic value in cod liver oil which are not disclosed by the specific tests for vitamins A and D. The concentrated *Oleovitamin A and D* represents for the most part a combination of the *Oleovitamin A* and the Synthetic *Oleovitamin D*. The dose of only 0.1 cc (or about 5 drops) of this represents approximately 5000 units of vitamin A and

1000 units of vitamin D and is equal to about 2 teaspoonfuls of a good grade cod liver oil

A fat soluble vitamin that is now newly added to the U.S.P. is *Menadione* (also as tablets), a substance with antihemorrhagic activity of vitamin K. Vitamin K analogues have also found a place in the 3rd supplement to the B.P.C. under the names menaphthone and acetmenaphthone. Menadione is 2-methyl-1, 4-naphthoquinone and possesses even 3 times the antihemorrhagic activity of the natural vitamin K, isolated from Alfalfa and shown to be 2-methyl-3-phytyl-1, 4-naphthoquinone. After it became known that vitamin K activity was found in quinoid compounds, a number of synthetic quinoid compounds were studied and Menadione was found to be the strongest. These substances when given by mouth are absorbed through the upper part of the jejunum, but the presence of adequate amounts of bile (salts) is required for the absorption of the vitamin. It may be noted that excessive amounts of liquid paraffin taken with meals may prevent the proper absorption of vitamin K. The richest sources of the vitamin are green leaves and vegetables (like spinach), mainly chlorophyll containing parts of plants. It does not appear to be stored in the body and what little is stored is in the liver. It appears to be associated with normal physiological function of the liver and with proper coagulation of blood. It is necessary for proper formation of prothrombin and its deficiency produces a deficiency of prothrombin in the circulating blood. Except when liver is severely damaged, the deficiency can be corrected by proper administration of vitamin K or its synthetic analogues. The minimal requirement appears to be very low and a dose of 1-2 mgm of Menadione will probably be sufficient in most instances (however depending on the degree of hepatic damage). No untoward reactions have been observed from the reasonable therapeutic doses. In adults it is indicated in all conditions associated with a deficiency of prothrombin in the blood, which may be due to inadequate diet or deficiency in intestinal absorption (from absence of bile salts or extensive intestinal lesions or diarrhoea in sprue, colitis, etc.) or injury to the liver. It may be given orally (with bile, if it is absent in the intestine) or there are some water soluble compounds like 4-amino-2-methyl-1-naphthol hydrochloride which can be given orally without bile salts. This and other compounds can be given parenterally (intravenously or intramuscularly). In the new born infants there is a (physiological) deficiency of prothrombin during the first week or so and the administration of menadione to the mother is recommended, in 2 mgm doses orally, a few hours before delivery to prevent hemorrhagic diseases or accidents of the new born. Vitamin E is still another fat soluble vitamin. It has not yet found a place in the U.S.P. But it or its analogue is included in the 3rd supplement to the B.P.C. under the name of Tocophenyl acetate. There is not sufficient evidence to show that vitamin E deficiency occurs in humans. It is, however, claimed that muscular dystrophies respond to vitamin E medication.

Vitamin B-complex is the most important group of water soluble vitamins and the most important source of these vitamins is yeast. *Yeast* and *yeast tablets* have now been included in the U.S.P. *Rice Polishings* are another crude source of vitamin B and are important in the history of the development of our knowledge of Beriberi. These ("Tiki-tiki") and an *Extract of Rice Polishings* is also added to the USP. For the treatment of alcoholic polyneuritis, the Beriberi heart and a variety of conditions associated with vitamin B₁ deficiency, both the BP and USP now provide pure vitamin B. The 1st addendum to the BP had added an adsorbate of this vitamin upon Fuller's earth from rice polishing or yeast or wheat embryo for oral administration under the name of *Pulvis Vitamini B₁* and the 3rd addendum afterwards added the pure substance in the form of *Thiamine Hydrochloride* (also as tablets and an elixir) with an average daily dose of 5 mgm. The elixir is not a good preparation because such liquid preparations are unstable.

Nicotinic acid is the most important single member of the "B" complex responsible for the curative effects of yeast, liver preparations etc. in the multiple deficiency disease called pellagra and it is added to the BP by the 4th addendum. It is included in the new USP under the name *Niacin*, in order to avoid any confusion with nicotine (the alkaloid in tobacco), with an average dose of 25 mgm, though larger doses are often used. Niacin often produces flushing, itching and burning of the skin with a small increase in cutaneous temperature, the effect occurring approximately half an hour after its oral administration. This reaction can often be avoided by using smaller but more frequent doses or by the use of nicotinic acid-amide also added to the USP under the name of *Niacinamide* with similar dosages. This amide is about 60 times as soluble in water as the acid itself and the side actions are much less pronounced after it. At present both Niacin and its amide are included in the USP because it is not yet satisfactorily established that the two are in all respects interchangeable in therapy.

Riboflavin or vitamin B₂ or G is another member of the B-complex added to the USP. It is apparently an essential constituent of the yellow oxidation enzyme. Spontaneous riboflavin deficiency in humans has been reported. The deficiency may cause ocular manifestations. The vitamin is probably valuable as an adjuvant in the treatment of multiple deficiency states such as pellagra. The ocular manifestations in deficiency include photophobia, dimness of vision, congestion of the sclera, vascularisation and opacities of the cornea, interstitial keratitis and these have been treated successfully with this vitamin.

(To be continued)

The Indian Physician

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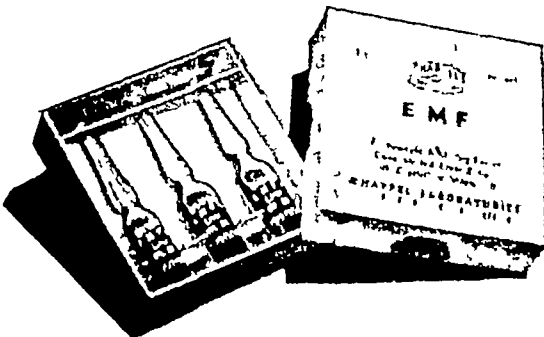
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Let us remember

THE PHYSICIAN IN THE MOURYAN EMPIRE

4TH CENTURY B C

By

D V S REDDY

Indhra Medical College

VIZAG

THE MEDICAL PROFESSION

The presiding deity of the Medical Art and Science —One additional proof that the Dhanvantari cult is a later development of the Puranic Age is evident from the Arthasāstra. Describing the location of the apartments for the worship of Gods in the very centre of the city, the book mentions that among others Siva and Aswins (the Celestial Physicians) had shrines (Bk I ch 4). Dhavantari is not even referred to, anywhere in the treatise. One may argue that Dhanvantari may not be the deity popular and famous in the Mouryan Empire at the time of the composition of the work. The cult may have come into vogue in other centres of Hindu Culture, particularly Kashi (Benares), associated with the name of Dhanvantari and his school.

Physicians and their wages —In the section dealing with rules regarding slaves and labourers, the question of the remuneration to the physicians is considered. And the clubbing together of "artisans, musicians, physicians, buffoons, cooks and other workmen" serving of their own accord, indicates that the medical men were treated as workers. They were to get wages and the scale and the penalty for non-payment are stated in the following words —"As much wages as similar persons employed elsewhere usually get or as much as experts shall fix", "Failure to pay wages shall be punished with a fine of 10 times the wages or 6 panams" (Bk III ch 13).

The state or the King, endowed lands to Physicians "Superintendents, Accountants, Gopas, Sthanikas, Veterinary surgeons, Physicians, horsetrainers, and messengers shall also be endowed with lands which they shall have no right to alienate by sale or mortgage" (Bk II ch 1) In this context, the reference may be to the Royal Physicians, State Physicians, etc

There was a separate category—"the physicians of the army" They were paid 2,000 panams per annum It is interesting to compare the scales of pay and allowances of different state officials

Minister commander of the army	18,000 panams per annum		
Collector, general Chamberlain Chief Constable			
Superintendent for Harem	21,000	"	"
Chief of military corporations of elephants, of infantry	8,000	"	"
Superintendent of infantry of cavalry	1,000	"	"
Chariot driver, trainer of horses physicians of the army	2,000	"	"
Soldiers accountants writers	500	"	"

Duties, responsibilities and privileges—The Royal physicians had very heavy burdens and rare privileges Before the king came to the Court, soon after getting up and receiving benedictions from priests and teachers, he had to see his physicians in his private rooms Even in the court, or having seated himself in the room where sacred fire has been kept, the king "shall attend to the business of physicians and ascetics practising austerities and of those who are experts in witchcraft and yoga" (Bk I ch 19) After narrating how kings were poisoned by their kith and kin and describing in detail how to detect poisons in food and poisoners, Kautilya cautions as follows, "Hence, Physicians and experts capable of detecting poisons shall ever attend upon the King" Even with regard to the taking of medicines, the following rule had to be observed, "Having taken out from the store-room of medicines that medicine, the purity of which has been proved by experiment and having himself together with the decoctioner and purveyor tasted it, the physician shall hand over the medicine to the king" The same wholesome rule applied to liquor and other beverages given to the king (Bk II ch 21) The ordinary physicians, too, had their professional responsibilities It would surprise the modern reader to note that a form of compulsory notification (as under the latest Public Health Code) was insisted even in that age "Any physician who undertakes to treat in secret a patient suffering from ulcer or excessive unwholesome food or drink,

as well as the master of the house (wherein such treatment is attempted) shall be innocent only when they (the physician and the master of the house) make a report of the same to either Gopa or Sthanika, otherwise both of them shall be equally guilty with the sufferer" (Bk II ch 36)

Another equally modern conception relating to the professional liability for damages is reflected in the section on "Medical Practice" Students of medical history may see its resemblance to the code of Hammurabi of the ancient Babylonians "Physicians undertaking medical treatment without intimating to the Government the dangerous nature of the disease, shall, if the patient dies, be punished with the first amercement If the death of the patient under treatment is due to carelessness in the treatment, the physician shall be punished with the middlemost amercement Growth of disease, due to negligence or indifference of a physician, shall be regarded as assault or violence" (Bk IV ch 1)

Those who go out at night in order to attend to the work of midwifery or medical treatment, were allowed to go about their work whereas others without special type of urgent work or passes, were not permitted to move about in the middle of the night and were liable to be arrested The medical profession was a privileged class In the section on the preparation for the battle, the work of the army doctors is outlined "Physicians with surgical instruments, machines, remedial potions and beverages should stand behind uttering encouraging words to fighting men" (Bk X ch 3)

Guise of a Physician seems to have been very frequently employed, and permitted for certain methods of statecraft This is another indication that the physician was respected, believed and was eagerly welcomed as a benefactor "A spy under the guise of a physician may make a seditious minister believe that he is suffering from a fatal or incurable disease and continue to poison him while prescribing medicines and diet to him" (Bk V ch 1)

"A spy under the garb of a physician may declare a healthy person of seditious character to be unhealthy and administer poison (Bk V ch 2) The Prince, hiding from his father or driven out by his father, may present himself when opportunity occurs, disguised as a physician or a courtbard and appeal to him (Bk I ch 18) Spies under the disguise of physicians acted

as agents for the envoy in foreign kingdoms to ascertain the nature of intrigue prevalent among the parties and the loyalty or disloyalty of the people in the kingdom in which he was staying" (Bk I ch 16)

Privileges of the sick and afflicted —The king was personally "to attend to the business of gods, of brahmans learned in the veda, of the young, the aged and the afflicted and helpless" (Bk I ch 19) Law judges dealing with criminal offences should not inflict fines and punishments of the same kind or degree on all people alike, among the people who should be shown mercy were included not only pilgrims and ascetics but also persons suffering from hunger, thirst and fatigue and diseased persons. Similarly, though there may be no actual complaints from the victims, the judges themselves had to settle transactions which pertain to gods, brahmans, minors, aged persons and diseased persons" (Bk III ch 20) Labourers suffering from disease were also to be shown concession or allowed to have the work done by a substitute (Bk III ch 14) The afflicted, the children and aged were provided with free passes to cross rivers "On the days to which birth star of the king was assigned, etc, such prisoners as are young, old or diseased, helpless, shall be let out from jail" (Bk II ch 36) Though torture to elicit confession was officially approved, a sensible restriction was added, "The aged, the afflicted, persons under intoxication, lunatics, persons suffering from hunger, thirst or fatigue, persons who have taken more than enough meal, or persons who were very weak—none of these shall be subjected to torture" (Bk IV ch 8)

Witchcraft —Steps were taken against persons engaged in such witchcraft as is hurtful to others. These wicked men living by foul means were treated as criminals. The belief in witchcraft was very common till recently even in Europe. It dominated the thought and actions of the nations and societies to varying extent. "Whatever a man attempts to do to others by witchcraft shall be practically applied to the doer himself" Witchcraft to arouse love in an indifferent wife or in a maiden was not considered an offence but when it is injurious to others, the doer was punished, for example, a man performing witchcraft to win the sister of his own father or mother or the wife of a preceptor or his own daughter-in-law, then his limb was to be cut off and he was to be put to death (Bk IV ch 13) "Whoever is believed to secure for others the love of women

by means of magical charms, drugs, ceremonials, performed on cremation grounds, may be approached by a spy with a request that the wife or daughter of someone whom the spy pretends to love may be made to return the love. If he consents to it, he shall be proclaimed as one, engaged in witchcraft and banished" (Bk IV ch 4)

Hospitals and their location —Another interesting record preserved in this book is the allusion to the Hospitals in India in the 4th century B C. Primers on the history of India never tire of telling that it was Asoka, the Great, that first provided facilities for the treatment of men and cattle. Kautilya's statement should be sufficient to prove the existence of hospitals in India before the time of Asoka. Hospitals must have been more than curiosities or novel innovations, if a book on Arthasāstra mentions the usual allocation of site in the Fort for the building of a hospital. "To the northwest, shops and hospitals." It would be interesting if one could conjecture the reason for this special site. But, one cannot help admiring the town planning experts, who went into such details, when even the 20th century cities have no such clearcut plans.

MATERIA MEDICA AND PHARMACY

Herbariums —It was a common practice to encourage the cultivation and storage of plants of medicinal value. "Such medicinal herbs as grow in marshy grounds are to be grown not only in grounds suitable for them but also in pots, marginal furrows between any two rows of crops were utilised for planting medicinal herbs. Vegetables and roots were grown in the vicinity of wells. In the discussion on the two watery tracts, one of limited area suitable for grains and another of vast area but productive of crops other than grains, the author adds that the latter of the two is better, "inasmuch as it affords vast area to grow not only the spices and other medicinal crops but also to construct forts" (Bk VII ch 11)

Customs duty or toll on medicinal articles —

Roots and bulbs (generally useful as medicines)	1/6 part
Articles like Arsenic sulphide (Hentala)	1/10
Red Arsenic (Mansila) Vermillion (Hingula) and Metals (loha) Pungents (Katuka)	1/15
Scents Medicines, Oils Sugar, Liquor	1/20 to 1/25 part (Bk II ch 22)
Commodities intended for confinement of women were let off free of toll (Bk II ch 21)	

Adulteration punished —Adulteration of scents and medicinal articles with similar articles of no quality shall be punished with a fine of 12 panams (Bk IV ch 2)

Variety of drugs —Since the book is not a treatise on Medicine, no direct references occur to the actual preparation of medicines from the various ingredients. But indirect evidence is abundant to suggest that the people had a large variety of drugs and also had knowledge of many interesting pharmaceutical processes and procedures. The section on mining operations and manufactures indicates the state of knowledge not only in mining, identifying ores, refining metals but also in softening metals, distillation, and condensation of mercury, formation of various types of alloys and many other metallurgical processes, that would surprise the reader. All this work was under the direction of a superintendent of mines. In addition, there was a superintendent of Goldsmiths to test the purity of the metals (Bk II ch 12, 13, 14). The superintendent of forest produce collected not only timber but also many useful articles especially medicines and poisons. "Bulbous roots and fruits are in the group of medicines." The following vegetable poisons were collected. "Kalakuta, vatsanabha, halahala, meshasring, musta, kustha, mahavisha, vellitaka, guarardra, balaka, markata haimavata, kalingaka, daradaka, kolasaraka, ustraka, etc." Likewise, snakes and worms kept in pots formed another group of poisons. The forest produce included metals, like iron, copper, lead, tin etc., and animal substances like bones, bile, teeth, horns, hoofs of various animals, beasts, birds and reptiles (Bk II ch 17). Among the articles to be stored in the fort in such quantities as can be enjoyed for years together without feeling any want are mentioned "Medicinal articles and poisons." Of such collections, old things shall be replaced by new ones when received (Bk II ch 4).

There was a superintendent of storehouse to store articles brought in by other departments such as the agricultural department. "Of the store thus collected half shall be kept in reserve toward off calamities of people and only the other half used. Old collections shall be replaced by new supplies. An idea of the type of articles stored is given by the long lists. The phraseology classification of the articles is reminiscent of the Ayurvedic

- (1) Oils (Sneha)—including serum of flesh, pith of plants, etc.
- (2) Sugar (Kshira)—including sugarcandy, jaggery and decoction of sugar.

- (3) Salt (Lavana) { Saindhava (rock salt), Yavakshara (nitre),
Samachal, Udhedaja, samudra, etc.

- (4) Madhu (Honey)—grape juice
- (5) Acid fruits—Myrobalam, etc
- (6) Pungent substances (Tikkavarga) long pepper, black pepper, ginger, kiratatikta, damanaka, maiuvaka, sigru, etc, with their roots
- (7) Edibles (Sakavarga)—Dried fish, bulbous roots, fruits, vegetables
- (8) Astringents (Suktavaiga)—Mixtures of juice of sugarcane, honey, etc, and of essences of fruits, jambu, myrobalam, etc,

(Bk II ch 15)

Preparation of spiritous medicines —Families were allowed to manufacture "Arista" for use in diseases and the superintendent of liquor collected licence fees from these people. The preparation of various kinds of "Aristas" for various diseases had to be learned from physicians. It is stated that one hundred palas of kapitha, 500 palas of phanita and one prastha of honey form "Asava". Many interesting instructions are given to prepare a variety of medicinal drinks as well as intoxicating drinks (Bk II ch 25)

References to certain diseases and medicines —Apart from the scattered references in the book to medicines and diseases, a whole chapter (Bk XIV ch 6) is devoted to "remedies against the injuries of one's own army". Herein, Kautilya deals with various preparations (with their ingredients) used as remedies against poisons and poisonous compounds, applied by an enemy against one's army and people. The following are mentioned:

- (1) Decoctions which are applied for washing off bad effects of poisons
- (2) Mixtures for removing the bad effects of poisoning by the madana plant
- (3) Mixtures to remove madness
- (4) Mixtures applied through the nose as "nosedrops" to remove leprosy
- (5) Mixtures to remove consumption
- (6) Nosedrops to remove headache and other diseases of the head
- (7) Mixtures (with doses) to resuscitate persons who fall down senseless, when beaten or by drowning or poisoning
- (8) Strange and miraculous medicines are also mentioned such as a powder for enabling one to see clearly in darkness and a powder enabling persons to fast for a month

In addition to drugs, mantras and other magical procedures were frequently used for protecting oneself and for hurting the enemy.

Original Contributions

THE AGE FACTOR IN THE LOCALISED ASEPTIC NECROSES

By

DOZENT Dr. GEORGE POLITZER

With 1 table and 2 x ray figures

From the Princess Surrendra Kumari Memorial Central X Ray Institute, Patnala

The use of x-rays for the diagnosis of bone and joint diseases led to the discovery of a group of diseases which have some important features in common

1 They are each one localised into a circumscribed and well defined area of the body

2 They occur during a limited period of life, and this period is characteristic for each disease

3 They are of non-inflammatory nature as proved by clinical, radiological and bacteriological researches

4 The bone changes are due to necrosis as ascertained by histological examinations

5 Generally the clinical symptoms are not of a grave nature, and many of these diseases pass unnoticed for longer or shorter periods

The excellent textbook of x-ray diagnosis by British Authors published by H K Lewis & Co, London 1939 gives a good description of these diseases illustrated by a table which I reproduce below. This table does not show the frequency of the different diseases only the diseases of *Scheuermann*, *Kienboeck*, *Koehler*, *Perthes-Legg-Calvé*, *Osgood-Schlatter* and *Freiberg-Koehler* are found rather often, while all others are rarities. For long difficulty has been experienced in finding a proper title for a chapter dealing with these diseases. The textbook quoted above heads this chapter by "Osteochondritis". This expression is rather misleading as the suffix-itis is meant for diseases of inflammatory nature to which the above diseases do not belong. Thus the title used in this paper "localised aseptic necroses" is surely preferable inspite of its inconvenient

length Another difficulty is faced when denominating each of these diseases To call them after the authors does not inform the reader of a report which area of the body is concerned Moreover, questions of priority are under dispute For example, Alban Koehler devotes pages 116-118 of the second edition of his Roentgenology to such a quarrel with Freiberg who undoubtedly described the disease of the head of the metatarsal bones earlier than Koehler, although the latter has added essential details to our knowledge Also the above chart contains a clear mistake quoting the name of Brailsford in connection with the disease of the scaphoid of the tarsus of the adult as three cases of this disease were described by Osborn, Weiss and Mueller years earlier In my opinion the best solution is to quote the authors' names together with the area concerned, as for Kienboeck's disease of the semilunar bone or Koehler's disease of the scaphoid of the tarsus

TABLE

SPINE	PRIMARY CENTRES	SECONDARY CENTRES
	VERTEBRAL BODY (Calve 1925)	EPIPHYSEAL PLATES (Scheuermann, 1921)
Upper Limb	ADULT Semilunar (Kuenboeck 1910) Scaphoid (Preiser)	Clavicle, Sternal (Friedrich 1924) Humerus Head (Lewin 1927) Humerus Capitellum } (Brailsford 1935) Radius, Head Ulna, Distal (Burns 1931) Metacarpals Heads (Mauclaire 1927)
Lower Limb	Patella Kohler 1908 Astragalus (Mouchet, 1928) Scaphoid (Kohler 1908) Medial Cuneiform (Buschke 1934) ADULT Scaphoid (Brailsford 1935)	Iliac Crests (Buchman 1925) Pubic Symphysis (Van Neck 1924) Ischiopubic Junction (Vollmar 1925) Acetabulum (Brailsford 1935) Femur Head (Perthes Legg Calve 1910) Femur, Neck (Gulig and Hertzog 1932) Femur Trochanters (Monde Felix, 1922) Patella, Polar (Sinding Larsen 1921) Tibia Head (Ritter, 1929) Tibia Tubercle (Osgood 1907) Os Calcis (Sever 1912) First Metatarsal Proximal (Wagner 1930) Second and Third Metatarsals Head (Freiberg 1914)

The histological findings in all these diseases leave no doubt that the changes are due to subcortical necrosis of the bone with subsequent compression of the cortex Axhausen in particular has examined histologically all the important diseases of this group and the ample data published in his papers leave no doubt of the correctness of his interpretation Also the

experiences collected by me in cases of *Kienboeck's* disease of the semilunar bone tally well with the findings of that author. Only as far as the later changes are concerned there is a wide variation in the clinical, radiological and histological findings and this is the point to which this paper relates.

Let us consider the clinical and radiological features of one of the best known diseases of this group, the *Perthes-Legg-Calvé's* disease of the femoral head epiphysis.¹ The disease is found in children between 3 and 14 years the highest incidence being between 6 and 8. The head of the femur becomes flat and condensed. Later it often disintegrates, forming two or more fragments. The upper half of the joint space is broadened. The rest of the joint facets remain smooth and normal, although occasionally the lateral part of the roof of the acetabulum may show changes similar to those seen in the head of the femur. The intactness of the major part of the joint facets and the absence of diffuse decalcification of the constituents of the hip joint are evidence against the idea that the condition is of an inflammatory disease. When the acute stage of the disease is over, the surface of the affected parts of the joint becomes smooth again, the structure becomes entirely normal and the only remnant of the disease is the deformity of the head which is described as roller- or mushroom-shaped according to the various types observed. Clinically, the overwhelming majority of the "cured" patients feels entirely well. But after the lapse of 10 years or more, some slight pains may occur again. The radiological examination now reveals the presence of small exostoses at the borders of the joint constituents, as in cases of secondary arthrosis deformans. These changes are easily to be explained by the fact that all joints with deformed constituents react on protracted use by arthrosis deformans whatever the origin of the deformity may be (post-traumatic, post-inflammatory, congenital, malacic a s o).

Quite different is the history of cases of *Kienboeck's* disease of the semilunar bone of the wrist. The disease is found in adults usually between 25 and 40 years. Radiologically the semilunar bone is compressed in a disto-proximal direction and condensed. Later, fragmentation may occur. Sometimes, one of these bone fragments locks the joint and thus necessitates surgical interference. The further observation of the patients

shows that whatever treatment may be adopted, reparative changes are only slight or absent. Neither the form nor the structure of the bone returns to normal. The patient never becomes fully free from pain, which may even increase later due to secondary arthrosis deformans, a sequel which also cannot be prevented by early or late operation (removal of the semilunar bone or its fragments).

The course of the above two diseases is thus very different. *Perthes - Legg - Calvé's* disease shows complete restitution of the normal structure and a clear tendency to at least partial recovery of the normal form, while the reparative processes in *Kienboeck's* disease are extremely poor, often non-existent. Let us summarise the experiences in other diseases of this group. The *Freiberg-Koehler's* disease shows primarily a good recovery of the structure but the persistence of a mushroom-shaped deformity of the head of the metatarsal bone. Due to the extensive mechanical use of the joint, the secondary arthrosis deformans often reaches quite extraordinary degrees. *Osgood-Schlatter's* disease and *Koehler's* disease of the scaphoid sometimes heal and leave no trace and a similar splendid result I found once in a case of *Calvé's* disease of a vertebra. All these diseases affect children of various ages. *Freiberg-Koehler* 10-15 years, *Osgood-Schlatter* 12-15 years, *Koehler* 3-10 years with a decided peak incidence at 5-6.

This shows that the diseases of the children lead to far better end results than the diseases of the adults, even the same disease shows a tendency to recovery with the age of the patient. Moller has proved beyond doubt that the end result in cases of *Perthes - Legg - Calvé's* disease depends chiefly on the age of the patient at the time of the attack. In very young children the results are often such that no traces of the former disease remain, while in older children roller- and mushroom-deformities prevail. Another observation has been made by many authors who have studied numerous cases and I can confirm it by the observations I made myself in dozens of cases belonging to this group. In all the juvenile forms of these diseases other things being equal the result depends on the stage in which the cases came to the observation, and on the stage in which the affected joints were set at rest by plaster casts or similar appliances. This is not true for *Kienboeck's* disease of the semilunar bone which affects adults only. The

course of this disease can hardly be influenced by clinical measures, at least as far as the processes in the semilunar bone itself are concerned

Nevertheless it cannot be said that the prognosis of a case of localised aseptic necrosis depends on the age alone. There is no doubt that the end results in the *Osgood-Schlatter's* disease of the tubercle of tibia are far better than those in the *Perthes - Legg - Calvé's* disease of the hip joint although the former affects children of 12-15 and the latter children between 3-14 but mostly of 6-8 years. It must further be remembered that in adults the only disease of this group which is found in sufficient numbers to deduce final conclusions is *Kienboeck's* disease of the semilunar bone. The other few observations found in the literature deal with rarities encountered in one or two cases only so that it is difficult to form a sound opinion. Furthermore the well known diseases of the juvenile and the adult affect different joints and bones, so that it cannot be gainsaid that the difference in the course of the different diseases may depend on the site of the affection and not on the age of the patient. Surely, the site of the process plays an important rôle in another question connected with this problem, i.e., the occurrence and the extent of the secondary arthrosis deformans. In cases in which the affected bone forms part of a joint which is strained by heavy daily use, the secondary arthrosis deformans reaches very high degrees as in the *Freiberg-Koehler's* disease of the head of a metatarsal bone, while in extra-articular bones such as the tubercle of the tibia, no secondary arthrosis deformans occurs at all. Also in cases of *Kienboeck's* disease of the semilunar bone, secondary arthrosis deformans is sometimes only slight especially in well-to-do patients or in people who can limit the use of the diseased hand.

The importance of the site of the affection can only be decided finally when diseases of the same joints are found in the adult and in the child.

The *Koehler's* disease of the scaphoid of the tarsus has been observed in many dozens of cases and the good, sometimes splendid, prognosis of this disease has been clearly shown. Recently, some cases of necrosis of the scaphoid in adults have been described by *Osborn, Mueller, Weiss* and *Brailsford*. The cases of *Mueller* and *Weiss* were shown to me and I was con-



FIG 1

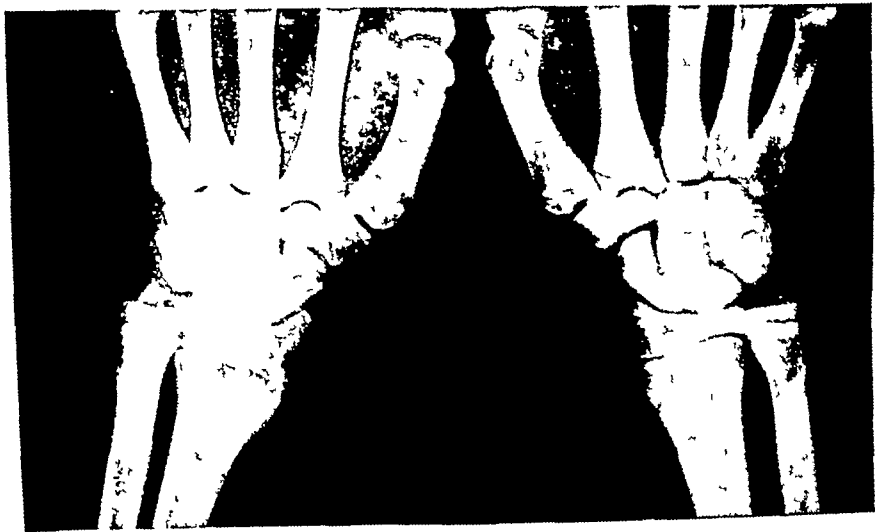


FIG 2

vinced that in these cases no signs of repair were present. But there is still a better argument to be deduced from our own observations and some reports published in the literature. It has long been known that necrosis of the head of the femur may occur in cases of fracture of the head if the fracture line lies in the medial end of the neck or in the head itself. This complication is dreaded by surgeons after reposition of the luxation of the hip joint. But it is less well known that similar cases of necrosis of the head occur also in persons with no history of trauma. I have observed 8 cases of this kind in Europe out of which two were bilateral. None of them showed any signs of regeneration of the destroyed head. The functional result as expected was very bad. I show in Fig 1 another case of such a localised aseptic necrosis observed recently in an adult male patient (the case has been sent to this institute by Dr Jagdish Singh, 1st Surgeon Rajendra Hospital). The diagnosis (aseptic necrosis of the head of femur) cannot be doubted, as the perfect condition of the surface of the rest of the head and of the whole acetabulum excludes any inflammatory disease. We can say that the non-traumatic aseptic necrosis of the hip joint has an extremely bad prognosis as far as the joint is concerned, while the *Perthes - Legg - Calvé's* disease of the juvenile shows quite a good prognosis, dimmed only slightly by the late occurrence of secondary arthrosis deformans. For this disease the importance of the age factor in the prognosis is thus clearly established.

It might be interesting to study juvenile cases of well known diseases in the adult. The only aseptic necrosis in the adult of which hundreds of cases have been observed is *Kienboeck's* disease of the semilunar bone, and therefore, I have long searched for similar cases in children. I could, however, find only one case about 15 years ago, of which I reproduce the skiagram in Fig 2. The left semilunar bone shows a typical compression in disto-proximal direction, and its structure is markedly condensed. There were then no signs of fragmentation. All my attempts to re-examine the patient during the following years were unsuccessful as he was free from pain and did not like to undertake the travel to Vienna for scientific reasons. I learned later on that he had joined the military forces.

CONCLUSION

After discussion of observations on cases of aseptic necrosis in various sites the following views concerning prognosis have been formulated

1 All cases in children show full recovery of normal structure and the affected bones show a tendency to recover their normal form, while cases in adults show no reparative processes worth clinical consideration

2 In similar cases in children the extent of recovery decreases with the age

3 In similar cases in children the chances of recovery increase with early diagnosis and treatment, while in similar cases in adults, early diagnosis and treatment have little or no influence on the course of the malady

4 The degree of the secondary arthrosis deformans developing earlier or later after the disappearance of the acute changes depends on the degree of the deformity and on the site

In the course of the discussion a case of aseptic necrosis of the semilunar bone of a child has been described, a disease so far unknown in the literature

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A review

RADIATIONS AND THE LIVING CELL

By

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Considerable advances have been made in the last few years in our knowledge of the methods of combating the various human ailments. Radiation Therapy occupies a very important and a highly promising place in our present-day armaments in treating these ailments. Primarily the methods evolved, are the result of practical clinical experience and therefore empirical. Medical science thus remains an "applied" science. Enormous amount of work is being done to liquidate this empiricism and to rationalize, to know the modes of actions of those methods. In the particular branch in question the same holds true. The complexity of the living organism and the innumerable possible reactions of external and internal factors specially render the task difficult.

To be able to use the radiations most successfully, it is essential to observe the nature of the biological reactions and to know the how and why of these reactions.

Our knowledge of the actions of radiations is far from complete. Considerable divergence of opinion exists among eminent workers in this field.

In dealing with the effect of radiations on living cells two separate considerations are imperative—the physical and the biological. An elementary consideration of the nature of radiations, their methods of production, etc., is essential. Radiations comprise of two varieties—Corpuscular and Non-corpuscular. These corpuscles are material particles, the Alpha rays—Beta radiation of radioactive substances and the newly discovered neutrons go to form these Corpuscular radiations. Non-corpuscular radiations are wireless waves, heat rays, visible light, ultra-violet, x-rays and Gamma radiations. These are electrical wave motions or a series of electrical disturbances.

following each other at very short interval of space and time. These are associated with magnetic wave motions. They are also conceived as beams of photons or quanta of energy. The conception of photons or quanta is packet of *energy particles* being shot out in all directions with the speed of light. These non-particulate radiations are conceived thus as—electromagnetic wave motions of beams of quanta (photons) of energy. Waves of very short wavelength correspond to photons of high energy content.

When these radiations strike material particles, a certain transference of energy from oncoming radiations to the recipient material occurs. That is, part of the radiations are said to be absorbed by the recipient material. When the recipient material happens to be a biological structure—the absorption of these radiations produces certain physiological and morphologic changes. How these changes—biological changes are brought about—remain still a matter of research and controversy.

How do these rays behave in absorbent material? The beam of λ -rays is made up of swarms of photons. Energy in each photon is proportional to the voltage applied to the tube. When the beam falls on the material a certain number of photons is absorbed. Each absorbed photon ejects an electron—which is called a photo-electron. Energy of these ejected electrons is equal to the energy of the photon. These electrons produce a trail of electrons in the material as they travel. The effect is of a very discontinuous nature and it is found that only a minute fraction of the molecules of the absorbent material is affected.

Under certain circumstances, alternatively, the photon may be scattered by the atom with which it collides—Compton effect. A portion of the energy of the photon is left behind in electronic form. These ejected electrons also produce a discontinuous train of ions. Energy in both types of absorptions, ultimately is concentrated in a small number of atoms.

Certain physical factors play a more or less important role in biological changes brought about in the tissues when exposed to these radiations. These are, the voltage applied to the tube, intensity and the total dose of the radiations, the time and spacial distributions of the radiations, distance of the irradiated material from the source of the radiations, etc.

Radiations are always injurious to the cells that absorb them. But the final effect depends on the intensity of the radiations. If the radiations are too intense the cells and tissues are completely destroyed, never to recover, if on the other hand the dose delivered is not lethal, the cells and tissues recover from the injury to a greater or lesser extent. Formerly it was believed that radiations have also a stimulating effect on tissues. No doubt, some quickening of physiologic activity is produced by Gamma and Roentgen rays. But this acceleration is only temporary and soon followed by injury or death. Recent work by Canti and his collaborators negatives any existence of acceleration of the process of growth and hence there is no direct evidence that weak radiations are able to stimulate growth (Packard).

Lethal Effect The lethal effect on cells is observed by certain morphologic changes occurring in the cells. These changes are not observable by the naked eye. They are microscopic. The irradiated cells undergo a vacuolation of cytoplasm, fragmentation of their nuclei and coagulation necrosis. These cells never recover. It is not surprising that tissue cultures could be killed by heavy doses—say 10,000 "r". But it is more surprising that profound biological changes could be produced in those very cells with something like a thousandth part of that dose.

When a non-lethal dose of x-rays is given, at first, although biological changes are occurring, none is visible. There is a latent period of biological activity in the cells during which there is no visible evidence of such activity. Soon, however, the changes are rendered visible when they pass through a period of increasing intensity. The translucent cells become at first granular and then turbid. The proteins are converted into simpler compounds, they form visible aggregates. The change is a reversible one so that if the injury is not too severe and if the stimulation ceases, the cell returns to its normal translucent appearance. Observations (A J R Oct '38—B J R August, '38) of the effects of radiations on protein solutions have shown that the most important change produced is the change in the solubility of the protein molecule. Solubility of the proteins after exposure is reduced so that they are more easily precipitated. But the change is not generally reversible. Re-

covery taking place in cells after irradiation, however, points to the presence of some degree of reversibility. But it appears that this change in solubility of the cell protein is not able to produce cell injury. The temperature of the tissue after irradiation is responsible for this. Strangeways and Failla have given the best experimental evidence for the suggestion that the injury of living cells, by Roentgen rays, may be influenced by the temperature subsequent to irradiation. It appears that the primary effect of the Roentgen rays must be followed by a definite temperature change before injury occurs. If this temperature change is prevented or delayed—a certain amount of recovery will occur.

Another of the most important effects produced by irradiation is a change in the hydrogen-ion concentration of the cell plasma. With this alteration in hydrogen-ion concentration is also observed an increase in the permeability of the cell membrane. Immediately after irradiation there is an increase in the acidity of the blood—probably as a result of the passage of acid from cells into blood circulation. Other changes observed are a decrease in cell respiration and increase of glycolysis (Packard). These are the primary physiologic changes. The morphologic effects produced are a consequence of these primary biological effects.

Inhibition of mitosis, production of mutations and death in the case of rapidly dividing cells are the main three effects produced by small doses. The effect on the mitotic activity of the cells is most pronounced. All mitosis is delayed. Although the effect on individual cells varies according to the phase of mitosis in which the cell is when exposed to irradiation. Cell which is actually dividing cannot be prevented from so doing even with very heavy doses, although after the division these cells may remain quiescent. Cells just about to divide, that is potentially active cells, are prevented from undergoing mitosis. Experiments of Spear and Glucksman on amphibian material confirm and closely resemble the results obtained by experiments on avian fibroblast in vitro and mammalian tissues *in vivo*. These experiments of Spear and Glucksman give considerable exact information about the biological response and the ultimate fate of cells exposed to radiations. A definite alteration in the ratio of the different phases of mitosis is observed. After

an analysis of the different phases of mitosis Spear and Glucksmann state that "the radiation causes a fall, first in the prophase and then in the meta-phase and later still in the telophase. The net initial effect is to postpone the onset of visible mitosis."

The reaction of the irradiated cells is very clearly seen in the moving picture films produced by the late Dr Cantù. The mobility of the sensitive cells is quickly lost. They later disintegrate with explosive violence. When not severely injured the cells regain their mobility and begin to divide normally. Sometimes the cell dies suddenly. Three attempts are made by the cells at the return to mitotic activity after irradiation.

The first attempt at the reappearance of mitotic activity occurs about three hours after the end of exposure. Six hours after exposures first degenerate cells make their appearance. Degenerate cells are seen only in the area of the cells undergoing mitotic activity. They represent cells which were on the road to division. These potentially active cells when killed by radiations form the mass of the degenerate cells. These degenerate cells show one of the three recognised complex of cellular changes —

(1) *Chromatopycnosis* Separation of the chromatic from the non-chromatic material of the nucleus—the degenerated nucleus then consists of a large vacuole with a single mass of chromatin.

(2) *Hyperchromatosis* The nucleus remains as a dark stained mass attached to the nuclear membrane.

(3) *Chromatolysis* Nucleus breaks down into fragments, and is dissolved undergoing a change in staining properties.

Nine hours after exposure there is evidence of another attempt, at the mitotic activity which is also accompanied by a rise in the number of degenerate cells.

After twelve hours a third attempt is made by the cells for the resuming of normal mitotic activity. This time the attempt is successful. There is a return to normal mitosis and the degenerate cells are reduced or disappear.

Cells in the resting stage and those actually in the process of division are little sensitive to radiations. Potentially mitotic cells—cells just about to divide—are the most highly vulnerable.

Radiations are responsible for another very profound effect

on living material That is the production of mutations Mutation means the sudden appearance in the offspring and continued transference from generation to generation of a new character—which is not present in the parent Living material undergoes a process of slow change from generation to generation This process of change is related to the occurrence of mutations Spontaneous mutations are a rare phenomena in nature It is found that Roentgen and Gamma rays possess the power of inducing mutations—thus bringing about a change in the structure and formation of the irradiated material Now it is well known that the transference of various characteristics of structure and formation is the function of thousands of different particles called hereditary particles These are ultra-microscopic particles arranged in linear fashion along the threads of the chromosomes which form the nucleus of a cell These are also known as “genes” They are regarded as the most fundamental elements of all living material Prof Muller says, “these many genes, lying in the chromosomes of the body cells, determine by their corporate action, the forms and the function of all parts of the body—first in the embryo and then in the adult”

Roentgen and Gamma radiations are the most effective instruments for the production of artificial genemutations Neutrons also have been shown to be similarly effective in producing mutations P W Whiting states that “the effect increase with increasing dosage and the influence is more potent than that of Roentgen rays if comparison be made in terms of roentgens” (A J R Feb, 1940) Ultra-violet radiation is also effective in causing mutations but here the difficulty is that of reaching the germ plasm Pollen cells in a single layer when exposed to ultra-violet rays, show single point mutation, an effect different from that produced by Roentgen rays Induction of mutation by any other method is not yet effectively demonstrated Both the induced and spontaneous mutations have two definite features in common Both of the mutations are recessive—that is they occur only in the second generation and most of these mutations are completely lethal, those not directly lethal have more or less detrimental effect

Germ cells of all varieties, when irradiated, give rise to mutation changes—spermatozoa, whether irradiated in the testis or outside, spermatogonia mature eggs, oocytes, oogonia,

The work of J H Paterson in the Texas Laboratory (1928) showed that these changes can also be produced in Somatic cells. Although, it follows from this that all cells can thus be changed by irradiation, the susceptibility of various cells to irradiation is not identical.

Irradiation can induce two distinct varieties of changes in the chromosomes and hereditary materials, namely abnormality of the distribution of the hereditary material and changes in the structure or composition of chromosomes or the genes themselves. The former may produce the phenomena of "non-disjunction" when a chromosome enters the wrong germ cell. Real alteration of the structure of the hereditary material again may be of two kinds. One is the change in the linear arrangement of the genes or hereditary particle within the fine fibre of the chromosome. The second change is the alteration in the composition of the gene itself. These are the changes known as the "gene mutations". "There is absolutely definite evidence that both kinds of changes can be produced in abundance by exposure to Roentgen rays" (Muller). These mutations may bring about marked visible morphological alterations such as changes in the bodily form and size, colouration, fertility and many others. On the other hand the morphological alterations may be quite inconspicuous. There is no distinction between the induced mutations as a class and these spontaneous ones. Both are recessive and hence do not show in the first generation. The great majority of them are completely lethal in effect, while most of the others are to certain extent detrimental to life. Recent work of Timofeeff and Rekovsky has, however, shown that a few of these mutations may not be detrimental to life and might in certain circumstances be favourable to life. Muller in corroborating this says that "the possibility of such mutations in nature, without irradiation, furnishes the bases of natural evolution". Considerable amount of unquestionable work by Muller, Pinter, Weinstin have elucidated many other facts concerning induced mutations. The mutations not only can be induced, but once induced they can also be reversed, the mutations are slightly influenced by temperature, starvation produces lower and anaesthesia higher mutation rate by irradiation. The two known factors which increase mutations are heat and irradiation, the former about 100% and the latter

about 15,000%, then controls spontaneous mutations. Bauer and Boveri suggested that cellular mutation might have an important aetiological relation to the cancer problem.

Fisher-Wasels produced further evidence in support of this suggestion. The reader might rightly question the relevancy of all this "Mutational verbiage" and doubt its usefulness in practical radiotherapeutics. The reasons for such an inclusion will soon be obvious. First, there is the danger of producing pathological mutations by unnecessary and heavy exposures of the sex glands not only of the patients but also of the operator. These mutated genes are recessive and, therefore, the effects would not be evident for generations. Another more important reason is that if as suggested by (BUFI), cellular mutations are one of the important factors in the causation of cancer, great precautions have to be taken while treating. There is a possibility that irradiation of normal and inflammatory tissues may give rise to cancer. Desjardins quotes the work of Lacassane and Vincent in this connection.

The biological effects on living material are determined by a variety of factors. These are the total doses administered, sensitivity of cells to radiations, the time factor, that is the total spread in time as well, whether exposure is continuous or spaced, the intensity of radiations, the area of tissues exposed, the power of recovery in the cells. The effect of different wavelength is a subject of controversy.

Cells vary in their sensitivity to radiations. Albers-Schonberg observed the great sensitiveness of genital organs as far back as 1903. In the following year Heinecke demonstrated a similar characteristic in the lymphocytes. Cells whose reproductive power is most pronounced are found to be highly sensitive. Also sensitivity varies inversely with their stability in form and function. Cells of the nervous system, which are highly specialised and which have very little power of reproduction are less sensitive. This forms the law formulated by Bergonie and Tribendon.

But this rule is true only in a general sense, for bacteria and yeast cells, although they are comparatively indifferentiated and possess a fair amount of the power of reproduction, are resistant to radiations.

Further, the susceptibility of a particular kind of cell is

not always constant. Dividing cells are more sensitive than non-dividing cells, and of the non-dividing cells, those about to enter the process of mitosis are more sensitive than those far removed from it.

Again, the radio sensitivity varies with the environment of the cell. Sensitivity of cells increases when subjected to cold and decreases in absence of oxygen. Decreased metabolic activity produces a decrease in radio sensitivity. It is very high when the metabolic activity is high as in developing seeds and rapidly growing tumors. Although, the physiologic state of the cells at the time of irradiation is a determinant of its radio sensitivity, it is not possible to make an unqualified rule that the metabolic activity and radio sensitivity are causally related. For, although liver cells have a high metabolic activity, they are comparatively more radio resistant.

Another important factor that determines the radio sensitivity is the state of hydration of cells. Protoplasm of protozoa is more fluid and also more sensitive. Petry found seeds soaked in water to be more sensitive than dry seeds. Generally, young and growing cells contain more fluid protoplasm and are found to be more radio sensitive. There is still another factor, which goes to determine the sensitivity of cells to radiation—how far does irradiation itself alter the radio sensitivity of cells? Tumor cells exposed to radiation and then inoculated into animals are observed to give rise to very slow growing tumors. Further, it is found that about two or three times the dose is required to prevent the growth of such inoculated tumor, than when the cells before inoculated are not irradiated. It is found however, that this alteration in radio vulnerability is closely related to the time factor. Effects of radiations may be same, or less, or more according to the time interval between various exposures.

Process of Recovery This relation of interval of time and the biologic effect is closely related to the existence of the power of recovery in the cells from the damage caused by the radiations. This power of recovery inherent in the cells comes into effect after the damage of any kind—heat, ether, radiations, etc.

When tissues are exposed to any injury the process of repair starts as soon as the damage is caused. If the injury is not lethal and slowly inflicted, the cells are more likely to recover.

Cells exposed to sub-lethal radiation, continue to grow and divide when the effect of radiation is past. Mitosis, arrested by irradiation, becomes re-established after a longer or shorter interval. Huge doses of 50 to 60 thousands can be given to Protozoon *Paramecium* for instance—without causing permanent injury. The organism stops moving but resumes its activity after the effect of irradiation has passed. Division of eggs—fertilized after irradiation, by normal sperms, is retarded than in those not irradiated before fertilization. This explains the presence of an inherent power of recovery in the cells. What is the basis of this “inherent” power of recovery?

It is held that the primary effects of irradiation, such as flocculation of proteins and change in the concentration in living cells are reversible processes. That is, if the injury is not marked and not continuous, there is a reversal of the primary changes and the cell returns to its normal condition. Recent work on the effect of radiations on proteins solutions and the relation of temperature changes to radiation effects have thrown more light on the subject. (J H Clarck, Packard, Dognon, Vintembeyer, Strangeways and Fell). Most striking change produced is a reduction in the solubility of the protein molecule. This is known as denaturation. Proteins are thus rendered less soluble and hence they precipitate, readily. Aside of the recovery process taking place in functionally active cells, all radiation denaturations are in general irreversible, and therefore, the protein of the living cells can no longer function as normal constituents, an important fact for consideration in the lethal effect of radiation on tissues. In spite of this observation, the recovery process is held to be the result of the reversal of this denaturation effect. Some other factors besides irradiation have come into play. Observations on the effect of the temperature on the irradiated cells could explain this assumption. Dognon and more specially Strangeways and Fell have observed that increase of temperature after irradiation showed complete absence of growth. It appears that the primary effect of irradiation on cells is accelerated and is followed by secondary change by increase of temperature and that with such a rise of temperature definite injury occurs. “If the secondary change is delayed or prevented by lowering the temperature—injury will be delayed and recovery occurs”. Also, “it is probable

that the Roentgen changes are reversible, because of the small amount of absorption. The changed protein molecules are here widely scattered and not concentrated in dense layers" (J H Cl A J R '38)

Recovery begins almost at once after the injury, it bears no relation to the magnitude of injury and the rate of recovery is exponential that it increases with time

Recovery process has a certain relationship with the intensity of radiations and thereby also the temporal variations. If the intensity is less, recovery keeps pace with the damage caused. If the intensity is high, time required to apply a given dose will be short. Now, the recovery could take place in a particular time after exposure. The time required to produce a given effect in a high intensity dose will be a small fraction of the time required for recovery to occur. To produce the same effect in the same dose of low intensity radiation, the time required will be longer than the time for recovery to occur.

Now, suppose a high intensity dose is administered which is just short of producing the biological reaction. If a small dose is given immediately after, the biological reaction will appear. If, however, a delay is caused in the application of this—the cells will undergo partial recovery from the effect of the first dose and to produce the same biological reaction a larger dose will be required. Thus it appears that there is a gradual diminution in the residual effect of a given dose *with time*. In considerations of effects of a series of doses and continuation irradiation, their occurrence has to be thought of. Here comes the concept of "the cumulative dose () which is the dose existing at any time—being the effective sum total of all radiations received, allowing for the diminution," owing to the recovery taking place in the cells (Lea). Even while the cells are under the effect of continuation irradiation, they are undergoing a process of recovery and this affects the dose to be applied to produce a given reaction.

Further, different cells have different recovery rates. It is most pronounced in cells which have a low reproductive rate and low metabolic activity. Such cells are, however, found to be more radio resistant. There is ground, here, for the assumption that the susceptibility of cells to irradiation is inversely proportional to their power of recuperation (Packard).

Time Factor Views held regarding the influence of time factor in the administration of a particular dose of Roentgen or Gamma radiations, are conflicting. Experimental and therapeutic observations show considerable difference in the effects of radiations when applied *continuously* and at the specified time intervals. These conflicting opinions fall into three chief categories (After Love)

- (1) The greatest biological effect is produced by the application of high intensity radiations in a short time
- (2) Maximum effect produced by protracted radiations of low intensity
- (3) Biological reaction is independent of the time of irradiation

Certainly, these differences could not be due to any defects in observation. They are due more to the fact that each particular observation is held as a categorical imperative by the respective group of observers. These observations are not mutually exclusive and each one will be found to be essentially correct "when considered strictly in relation to the particular conditions under which the experiments were performed." W. H. Love believes that these results form part of a "general and more inclusive theorem." He has been able to prove by an analysis of various observations on the significance of the time factor that the quantitative reaction of a given dose in a particular tissue may be one of the following three —

- (1) Reaction may increase with increase in time, reach a maximum, and then begin to decrease, or
- (2) The effect remains independent of the time and then begin to decrease, or
- (3) The effect may decrease continuously with time

Radio sensitivity of tissues is not a constant property. It varies considerably during the life cycle of cells, being most marked in the period of highest metabolic and reproductive activity. Naturally, biologic reactions of cells would be most marked when applied during this period. When radiations are applied continuously—all these are not equally effective as the cells are most of the time in a radio-resistant stage. When radiations are so spaced as to fall only during the phase of high activity, the reaction will be most pronounced. Hence, the influence of the time factor

It has been found possible, by the appropriate variation of the interval between successive exposures to radiations, to produce one of the three following effects (1) less radio damage than, (2) same effect as, (3) or more radio destruction than by the continuous application of radiations

Weak doses delivered over a longer period are decidedly less effective than intense radiations which act for a short time. Ju 1—by using inoculated tumours as test objects could show this clearly, and this was later confirmed by the work of Holthusen on reaction. It is possible to give a large total dose to the skin by dividing the dose than by giving the same dose in single exposure which would produce a severe reaction

The fact that division of dose could produce *the same effect* as the same dose given in single exposure is demonstrated. Spear by exposing tissue cultures to Gamma radiations has been able to show that the administration of a single dose in six hours, or in six doses of one hour each at 24 hours intervals, a similar lethal effect could be produced

Again a greater effect by divided doses than by a single exposure of the same dose is observed. Appropriate choice of the time interval is very essential. *Chromatin*

Alberti and Politzer, using amphibian larvae, Regaud and Felioux, using male rabbits for sterilization and Eidenow and Mottram, using Jensen's rat sarcoma, have all been able to observe greater effects by divided doses with proper spacing of irradiation.

Spear found that two doses of approximately "100 r" Gamma radiations applied to tissue cultures, spaced 80 minutes had a greater effect on mitosis than 120 "r" applied at once.

Mottram in his experiments on bean roots, found that spacing of two exposures, so as to irradiate the cells when mitosis was abundant, had a greater destructive effect, producing higher death rate, than when the spacing was 6 hours. In the latter case the second exposure occurred when mitosis was in abeyance. It was also found that the 24-hour spacing was more effective than when the same amount of irradiation was applied at a single exposure.

The reason for such an influence of spacing is that the tissues are not continuously in a state of radio sensitiveness, also previous radiation alters the radio sensitivity of cells. It is

possible that during the application of a single large dose the sensitivity of tissues falls, thus rendering the greater part of the dosage of little effectiveness

Effects of different wavelengths

The action of radiations of different wavelengths was upto the present an unsolved problem. Still, there does not exist a complete unanimity on this point. Did different wavelengths produce differential reactions on tissues?

Observations of the effect of various forms of radiation naturally lead to a belief in such a differential response. Biologic effect of the long and short V V Radiations are quite dissimilar. The soft Roentgen rays were found to possess more effect on skin than the hard rays. The former are destructive and the latter were supposed to be non-destructive. Some of the earlier workers believed that different wavelengths should be taken as different elements. It was in 1915 that Rost showed that these were identical in action. His opinion has been confirmed by recent work and it is now recognised by the majority of experimentalists that the qualitative reactions of more than one different wavelengths are identical. Cells respond to analysis— from green to Gamma—in much the same way. At the same time it is found that the radiations of short wavelength are more selective in action. A marked difference in sensitivity is observed in tissues when exposed to filtered gamma rays than when under the action of Roentgen rays. This dissimilarity is not due to any difference between the rays of different wavelengths. It is the difference in intensity produced by filtration that is responsible for this differential susceptibility of tissues. Regend's experiments have shown this quite clearly. Roentgen rays of low intensity could show the same difference as shown by filtered Gamma rays. It is a result, therefore, not of different qualities but of different intensities.

The results of the series of tests on *Drosophila* eggs by Simon and Packard are more illuminating as they include the effects of a number of different wavelengths not so far used. Packard, from the data obtained from his work of *Drosophila* eggs, concludes that if the doses are equal, the magnitude of the biological effect is equal, regardless of the wave-

lengths used within very wide limits. His survey of the literature on this problem shows that though this view is gaining ground it is not yet universally held. This is specially the case as regards the erythema reaction of the skin.

Skin tolerates a larger dose of hard than soft rays. This is the reason adduced for the lesser effect of the former on the skin. It is argued that if all wavelengths are equally effective, equal doses in Roentgens should produce the same effect. But a little fallacy is missed while so arguing. Hard rays are obtained by greater filtration, filtration reduces the intensity of the radiation-beam. A beam of hard rays has, therefore, a lower intensity and so to apply the same dose in Roentgens the irradiation will have to be continued for a longer period. But during this prolongation of irradiation sensitivity of most cells becomes progressively decreased. This alters the biological material under test. The significance of time factor, here is lost sight of.

Further Holthusen's work on this problem has led to a general agreement, specially among radiologists in Europe, that the erythema bears a quantitative relationship to minute intensity and total intensity but is independent of the wavelength.

The present trend for the use of high voltages in Roentgen therapy necessitates a further elucidation of the relation of biological reaction to wavelength. Hodges and Perry present their study of this problem in A J R 1939. They studied the effects of wavelengths on skin tolerance by experiments on rabbits and humans. This work has led them to the conclusion that for similar amount of absorbed radiation, there is little or no difference between unfiltered rays of 10 K V and 200 K V rays with 1 mm cu and 1 mm al filters. Also Miesher quoted by Webster found little difference between high and low voltage x-rays. Further Choul's method of low voltage therapy in superficial conditions has been found to give results similar to those obtained by radium. These are valuable evidences in favour of the view that provided the intensities remain the same, i.e. the quantity of radiations absorbed is identical, the magnitude of biologic effect is the same regardless of the wavelengths used.

Reactions of living cells to x-rays, Gamma rays, etc., have been fairly definitely known. The problem now remains is the *modus operandi* of these radiations. The writer expects to present a review of the various hypotheses put forward regarding the mode of action of these radiations, in a future communication.

Critical Notes and Abstracts

INTRACRANIAL ANEURYSMS

In an analysis of the clinical manifestations and pathological findings in cases of intracranial berry aneurysms, Richardson, J C and Hyland, H H (*Medicine*, 1941, Vol I, pp 1-77) have admirably expounded the anatomical, clinical and pathological aspects of this very interesting subject and have correlated in an extremely lucid fashion the various clinical and pathological aspects

The presence of aneurysms of the cerebral arteries have been recognised and pathologically described for nearly a century Labert in 1866 described some of the clinical manifestations and the occurrence of apoplectic attacks and pressure signs from such aneurysms was described by others but it was as late as 1923-24 that Symonds associated spontaneous subarachnoid haemorrhage with rupture of these intracranial aneurysms, and with the help of x-rays, angiography and the increased frequency of intracranial operations the diagnosis of such aneurysms has been very much facilitated to-day

The authors have made a study of 118 cases of spontaneous subarachnoid haemorrhage and 8 cases of large unruptured aneurysms in this paper

Spontaneous or non-traumatic subarachnoid haemorrhage may be of three types as described by From (1904) He spoke of (1) Primary subarachnoid haemorrhage, (2) Cerebrumeningeal haemorrhage, and (3) Meningocerebral haemorrhage But From made no contribution to the cause of the spontaneous subarachnoid haemorrhage Recently many writers have pointed out that spontaneous subarachnoid haemorrhage is in most cases caused by the rupture of an intracranial aneurysm The presence of angiomas, purpura, arteriosclerosis, pertussis, acute infections, intoxications and syphilis have been mentioned as other possible causes but the authors do not find any, excepting a solitary case of an angioma, as the causative factor

From a series of 34 cases of fatal subarachnoid haemorrhage in which an autopsy could be performed the authors find 28 cases, accounted for by the presence of aneurysms (though in one case the aneurysm was found out years after the autopsy from the specimen preserved in the museum) One case was accounted for by the presence of an angioma and in five cases no bleeding point could be found

The intracranial aneurysms may be (a) Congenital or developmental or "berry," (b) Mycotic, associated with septic endocarditis, (c) Miliary, of no clinical or pathological importance and occurring at the ends of the arterioles within the brain substance, (d) Arteriosclerotic, (e) very rarely syphilitic (there are only one or two recorded

cases in literature), and (f) Traumatic arterio-venous aneurysms resulting from fracture of the base of the skull. It is interesting to note that most of the intracranial aneurysms are congenital and that syphilis which is responsible for 90% of the aneurysms found elsewhere in the body is a very unusual cause of an intracranial aneurysm.

Covering the record of 4618 autopsies the authors found 40 cases of intracranial aneurysms, an incident of 0.87% but only in less than half of these was the skull opened up so that the real incidence would probably be somewhat higher. In this series of 40 cases, 18 were male and 22 female and their age varied from 21 to 89 years, majority being roundabout 50. In thirty cases the aneurysm was a single one, while in seven cases two aneurysms were seen and in three cases three aneurysms were detected in each. The aneurysm was found most often in the anterior part of the circle of Willis, 42 out of 53 aneurysms being seen there. 16 of these were seen in the middle cerebral artery in the sylvian fissure near its first or second branching, while 13 were at the junction of the anterior communicating with the anterior cerebral arteries. 11 were found around the bifurcation of the internal carotid artery whereas 2 were seen on the internal carotid before its bifurcation, 2 were on the posterior cerebral arteries. The aetiology of the formation of the aneurysms is not fully understood but the significant fact that they mostly occur at junctions suggests that a weakening of the media and an increase in the intravascular pressure, which are found at those points, might play a part in it.

Clinical Syndrome—The cerebral aneurysm may remain entirely latent and may be found on a routine post-mortem examination as in 9 of 40 autopsies reported by the authors. The aneurysm may, by virtue of its size and position, produce pressure symptoms and signs and may simulate an intracranial tumor but most often the aneurysm is small and produces no symptoms until it ruptures suddenly and produces its characteristic syndrome of spontaneous subarachnoid haemorrhage but on this may be superimposed manifestations of intracerebral haemorrhage, which is not infrequent.

From the survey of clinical observations in 126 cases the authors come to valuable conclusions regarding the clinical manifestations of the berry aneurysms.

Onset—In the great majority of the cases the onset was sudden, without any premortory symptoms, in a person apparently perfectly well, and during ordinary activity. In 10% the onset was prolonged over a few hours or even days.

Premortory Symptoms—Severe generalized headache radiating down the back of the neck frequently associated with vomiting, was the first symptom in a majority of the cases (83%). Loss of consciousness was the next most frequent manifestation at the onset. Convulsions are uncommon at the onset (9%).

Predisposing factors—In 50% there was no history of any symptom whatever, and no underlying disease, prior to the onset, while in the remaining, hypertension was the only constitutional disorder that

occurred with sufficient frequency to be regarded to be more than accidental. Migraine was not frequent enough to support the theory postulated by Adie (1930) that migraine is closely related to intracranial aneurysms which proceed to rupture. There was no case of ophthalmoplegic migraine which is supposed to be due to leaking aneurysms. In a few cases (six) the headache preceded the onset for some time ranging from a few hours to a few days. No history of trauma, infection or any other condition which could be regarded as a predisposing cause for the occurrence of the haemorrhage could be obtained with any constancy.

Clinical Examination —

(a) *Symptoms due to Subarachnoid Haemorrhage* — Usually there is mild general retardation of memory and attention but rarely severe mental disturbances occur without intracerebral involvement.

There is marked stiffness of neck associated with a positive Kernig's sign but actual head retraction is rare. The pupillary reactions may be sluggish and the tendon reflexes in the legs markedly diminished. Bilateral Babinski's response may be present and may disappear with improvement. There is a low grade fever and a mild leucocytosis. Papilloedema and fundal haemorrhages are more common in the severe and fatal cases. Subhyaloid haemorrhage also renders the prognosis grave.

The cerebro-spinal fluid is evenly blood-stained soon after the haemorrhage. The fresh blood disappears in from 4 to 19 days, the average being 6 days in the 24 cases studied from this viewpoint by the authors. Xanthochromia was detected as early as 12 hours after the onset and is usually present 24 hours after but in 2 cases it took 3 days before it could be demonstrated. The fluid returned to its normal clear colourless state in periods varying from 10 to 39 days, the average being 20 days. In several cases an increase in the mononuclears was noted in the spinal fluid in from two to four weeks after the onset, the counts ranging from 16 to 320 cells per cmm. Proteins and globulin are naturally found to be increased.

(b) Localising Signs of Intracranial Involvement

• It is usually stated in literature on subarachnoid haemorrhage that "there is no gross cerebral localization in these cases" or that "significant negative findings are the absence of hemiplegia, other focal signs, or choked disks". However it is often found that not only the involvement of the cranial nerves but the occurrence of the intracerebral haemorrhage with the corresponding localising signs is not uncommon in spontaneous subarachnoid haemorrhage. As many as 53% (62 patients) in this series had such local signs. The frontal and the temporal lobes are much more commonly involved than the other lobes and the parietal lobe, though rarely primarily involved, is often secondarily affected. The clinical syndromes vary with the extent and the situation of the haemorrhage.

Frontal lobe haemorrhage results from aneurysms of the anterior cerebral and anterior communicating arteries. The most frequent

signs are contralateral hemiparesis, varying from slight weakness to complete paralysis with aphasia. Intellectual retardation is the other principal finding and tends to persist after the other signs of subarachnoid haemorrhage clear off. If both the frontal lobes are affected from their mesial aspects there is severe dementia which is likely to be permanent. Cranial nerve involvement is not usual with frontal lobe haemorrhage. Involvement of the optic nerve is sometimes met with as manifested by transitory amaurosis or amblyopia.

Temporal lobe haemorrhage usually results from ruptured aneurysms of the carotid bifurcation or in the Sylvian fissure. The most constant sign is a homonymous visual field defect. In left-sided lesion aphasia with word-blindness is likely to be present. There is often an involvement of the 3rd or the 5th cranial nerve. If the bleeding spreads medially to involve the pyramidal fibres there results a hemiplegia which is often maximum in or confined to the face and if the sensory tract is also involved hemianaesthesia accompanies the hemiplegia. When bleeding extends distally into the ventricles by penetration of the genu of the corpus callosum there may be profound coma, dilated fixed pupils, and bilateral Babinski's sign. The 3rd and the 6th nerves are most often involved due to their proximity to the internal carotid and the middle cerebral arteries. The 5th is affected next in frequency and the 2nd, 7th and 8th were involved occasionally but the 9th, 10th, 11th and 12th cranial nerves were not involved.

(c) Symptoms of Large Unruptured Aneurysms

These bear close resemblance to the symptoms produced by cerebral neoplasms, being produced only by pressure of the gradually expanding mass and differentiation may only be possible by angiography or at operation. The patient has a history of headache of some standing with gradual involvement of the mental faculties and the paralysis of the cranial nerves according to the situation of the aneurysm which is most commonly on the internal carotid or the basilar. In the latter situation the progress is slow and there may be signs of a tumour in the cerebello-pontine angle with ataxia.

Diagnosis —The sudden onset of headache and loss of consciousness in a person previously healthy, without any exciting cause associated with signs of meningeal irritation and possibly diminished reflexes in the lower limbs suggests the diagnosis of spontaneous subarachnoid haemorrhage from aneurysmal rupture. When the cerebrospinal fluid contains blood and the supernatant fluid is xanthochromic after centrifuging, no doubt can exist regarding the diagnosis. Similarly sudden onset of cranial nerve palsy, usually oculomotor, in a person previously healthy, always suggests the possibility of intracranial aneurysm. If the accompanying signs of subarachnoid haemorrhage are slight and the patient is seen some weeks after the onset the diagnosis becomes difficult. Encephalitis, disseminated sclerosis, cerebral syphilis, and intracranial tumours may have to be considered but the sudden onset with severe headache usually enables the diagnosis to be made. Angiography with thorotrast has proved particularly helpful in such cases.

The real difficulty comes in differentiating intracranial lesions accompanying spontaneous subarachnoid haemorrhage from primary intracerebral haemorrhage. If the patient is conscious or if a reliable history is obtained, the severe headache and stiffness of the neck preceding the stroke favour the aneurysmal rupture. In primary cerebral haemorrhage the paralytic signs are present, right from the time the patient is first prostrated while in the aneurysmal rupture, they develop after a period of 1 to 12 days. The preservation of consciousness favours the spontaneous subarachnoid haemorrhage. In the absence of vascular hypertension the occurrence of cerebral haemorrhage, subarachnoid or intracerebral, should always suggest aneurysmal rupture as the basis. When a young person develops hemiplegia without obvious cause such as hypertension, neurosyphilis, or endocarditis, a ruptured berry aneurysm is the most likely cause, even in the absence of other signs of subarachnoid haemorrhage.

Cerebral angiomas are difficult to be differentiated but a murmur over the skull or the presence of facial naevi or the eye sign may help their recognition.

Large aneurysms have to be differentiated from cerebral neoplasms and although carotid aneurysms may be recognised by their characteristic signs, other situations are more difficult to localise. Only occasionally an x-ray may help by showing a calcified ring in the aneurysmal sac.

Prognosis—Approximately half of all the cases of spontaneous subarachnoid haemorrhage recover, yet in a given case the imminent prognosis may be difficult to assess unless the lesion is very mild or very severe. Increase in age and in blood pressure make the prognosis a little grave and the presence of subhyaloid or fundal haemorrhages add to the gravity. Unconsciousness at the onset is not necessarily of bad prognosis unless prolonged. The ultimate prognosis is good in cases once recovering, the patients having no residual symptoms or little if there is cerebral involvement. Gross destruction of the cerebral tissue will leave behind severe and permanent signs. Danger of repeated attacks is not very frequent, two or more attacks occurring only in 14% of this series.

Treatment—Complete rest in bed, not less than six or eight weeks in the mildest of cases, is most important. It must be enforced until all symptoms such as headache, stiffness of neck, vertigo, etc., have not been present for at least four weeks. The return to ordinary activity should be very gradual and strenuous exertion avoided for at least four months. Sedatives, nursing and diet should be attended to as required. Spinal drainage should be done slowly and only a small quantity of fluid removed only for the sake of diagnosis or if symptoms increase during treatment. Routine and regular spinal drainage is not called for. The surgical treatment is far from satisfactory at the present time.

M D M

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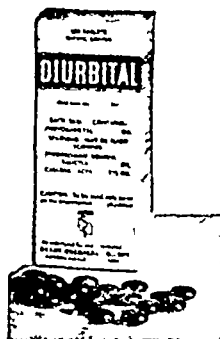
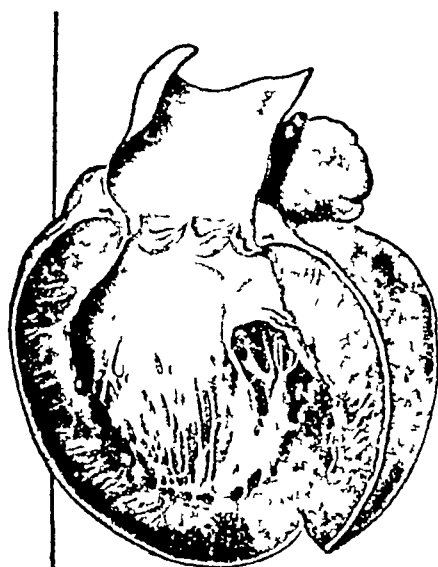


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Original Contributions

TROPICAL EOSINOPHILIA

By

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Weingarten (1943) described a clinical syndrome, called by him "tropical eosinophilia," which he had observed in 81 cases. It is characterized by leucocytosis up to 74,000 and an extremely high eosinophilia up to 89 per cent, accompanied by mild attacks of bronchial asthma and a characteristic radiological lung picture. Signs and symptoms respond very well to organic arsenicals. The only aetiological factor, common to his cases, was that all of them had spent some time on the West coast, prior to the manifestation of clinical symptoms—Treu (1943) reported two cases which apparently belong to the same group and Simeons (1943) stated that he has successfully treated several cases of this kind on the same lines.

Though we have seen a few cases, fitting to the clinical description of tropical eosinophilia, during the last three years, we diagnosed them as atypical cases of Löffler's syndrome and treated them as cases of bronchial asthma with the usual unsatisfactory results. During the last few weeks we encountered two cases of this type which responded so promptly to organic arsenicals that it seems justified to report them.

Case 1 S K, a Mohamedan merchant, 30 years of age was admitted to this hospital on 25-5-1943, mainly complaining of bouts of cough, accompanied by moderate dyspnoea and wheezing sounds, coming on during the small hours of the day, the cough being particularly unproductive. His history revealed that in August 1942, staying

then in Bombay, he fell ill with fever, headache and malaise, this acute stage subsided in about one week's time, leaving him, a previously strong and active individual, extremely weak and listless. A few weeks later in Bangalore, nightly cough started, disturbing his night rest to such an extent that he ascribed his inability to regain strength in spite of tonics, etc. to the insufficient amount of sleep. A blood count, taken in Bangalore, in October 1942, showed 38,000 leucocytes, a differential count was not done. A series of liver injections was administered without giving him any relief. Prior to the present illness he had been always perfectly healthy and, even now, he was convinced that nothing would be wrong with him if he could get rid of the "asthma" and thus secure undisturbed nights. Since 1940 every year he had to spend several months on the West coast (Calicut, Cannanore, etc.). One of his brothers was suffering from severe migraine attacks.

On admission, the tall, well built and well—but not over-fed young man presented the following findings. Respiratory system on percussion a moderate degree of hyper-resonance over both the lungs, on auscultation a few rhonchi and moist rales, scattered over both sides. Heart normal, pulse rate 84, blood-pressure 125/85 mm Hg. Spleen slightly enlarged with a firm, rounded pole, liver just palpable. Nervous system nothing abnormal.

Radiogram of the chest (26-5-1943) numerous round opacities of split-pea size with hazy margins are present, some of them showing diminished density in the centre. The maximum of this mottling is visible in the infraclavicular regions, bilateral in the peripheral parts of the middle zone and the lower lobes (Fig 1).

Blood count on 25-5-1943 total leucocytes 24,000. Neutrophils 34 per cent, eosinophils 52 per cent, lymphocytes 3, large mononuclears 11 per cent. Three day-and night-samples of blood were negative for filariasis. Malarial parasites absent, malaria flocculation test negative. Kahn-and Kline-reactions negative. Sedimentation rate (Westergreen) 10/27. Urine, chemically and microscopically nothing abnormal, on culture no growth. Motion, examined on four occasions, did not contain any pathological elements, especially neither ova nor cysts. Sputum was examined by concentration method every day from 25-5-43 to 7-6-43. Neither tubercle bacilli nor elastic fibers were present. On 30-5-43 and 7-6-43, when some larger amounts were expectorated, "plenty of eosinophils" were found in the sputa.

To exclude a spontaneous improvement due to the patient's coming from Bangalore to Mysore or owing to hospital conditions, treatment was not started before 28-5-43 when Novarsenobillon (NAB) M & B, 0.15 gm was intravenously injected. Prior to this first dose, the blood count was repeated and found almost unchanged, but for a slight increase in eosinophils from 52 to 55 per cent and a decrease of neutrophils to 29 per cent.

The table shows the further development of the blood picture under NAB therapy which constituted the only treatment of the patient.

HEILIG AND VISHVESWAR — TROPICAL EOSINOPHILIA

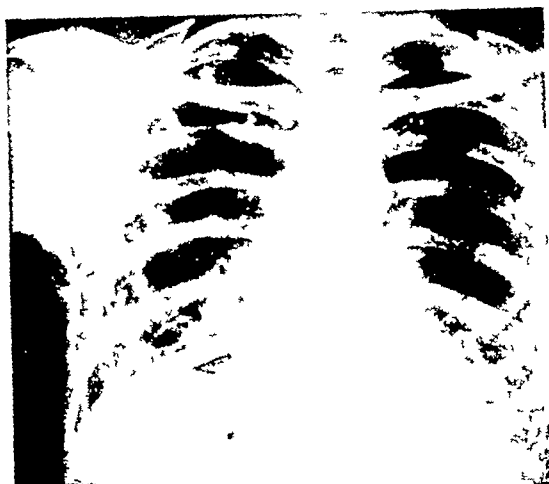


Fig. 1—Radiogram of the chest of case 1 taken before treatment on 26.5.43 showing numerous round opacities of split pea size with hazy margins some with diminished density in the centre. The maximum of this mottling is visible in the infraclavicular regions, bilateral in the peripheral parts of the middle zone and the lower lobes.

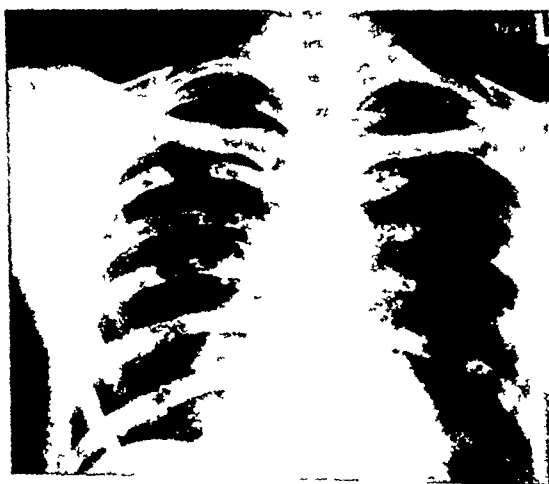


Fig. 2—Radiogram of the same patient, after treatment taken on 7.6.43 showing a definite clearing of the lung fields due to considerable reduction of the number of densities.

TABLE

Date	Leucocytes total	Neutrophils %	Eosinophils %	Lymphocytes %	Large monocytes %	Therapy
2-5-42	24 000	34	32	3	11	
28-5-42	24,500	29	55	2	14	N.A.B 0.15 gm
31-5-42	20 600	30	53	7	10	
1-6-43						N.A.B 0.3 gm
2-6-43	20 000	28	63	3	6	
4-6-43	20 400	26	64	3	7	
5-6-43						N.A.B 0.45 gm
7-6-43	20 100	21	66	3	10	
9-6-43						N.A.B 0.45 gm
14-6-43	14,200	40	37	20	3	N.A.B 0.45 gm
19-6-43	10 100	43	22	28	7	N.A.B 0.45 gm
23-6-43	5 000	48	14	31	7	N.A.B 0.45 gm.
29-6-43	4 600	65	9	22	4	
Total						N.A.B 2.7 gm

Already after the third injection (8-6-43), the patient lost cough and dyspnoea, from then onwards he had undisturbed nights and good sleep. The last, slight asthma-like attack he experienced on 7-6-43, when the sputum, the expectoration of which marked the end of the attack, still contained a considerable amount of eosinophils. A radiogram, taken on the same day, showed a definite clearing of the lung-fields, due to considerable reduction of the number of densities (Fig 2). The bronchitic adventitious sounds had completely disappeared by this time, although the leucocytosis was only slightly diminished and the percentage of eosinophils rose to 66 per cent. It took another three injections of N.A.B., 0.45 gm each, to reduce the leucocyte count to 5,000, the eosinophils to 14 per cent and one more dose to bring them down to 9 per cent.

Thus, the clinical and radiological improvement are not necessarily accompanied or conditioned by a normalized blood condition.

Case 2 R. S., Lingait, grain dealer, 32 years old, consulted us as an out-patient. Since about six years he suffered from attacks of cough, coming on once or twice a month, at about 1 a.m., since four years this cough was accompanied by dyspnoea and wheezing sounds. During the last two months the attacks became more frequent, appearing almost every night and making the use of ephedrine necessary, by the end of such an attack phlegm is expectorated which comes partly from the nose, partly from the chest. The patient stated that exposure to cold wind, taking an oil bath, at which occasion soap nut powder is habitually used, heavy food such as beans, and smelling of soap nut powder regularly causes his "asthmatic" complaints. He did not remember to have suffered from fever prior to or at the onset of his illness. Since the frequency of the attack increased, he felt weak and not inclined to strenuous work. Though he visited occasionally the West coast (Mangalore, Ernakulam), he definitely stated that he was never there prior to the beginning of his illness. At this time, however, he travelled frequently in the Malnad districts of Mysore, an extremely unhealthy, malarial area with heavy rainfall and dense jungle, situated at the inland slopes of the Western Ghats. Patient is the strictest vegetarian and non-smoker, he denied venereal infections.

The first examination (29-6-43) of the well-built, rather slim and tall man revealed a moderate emphysema, prolonged expiration, a fair amount of râles, rhonchi and some wheezing sounds. The spleen was slightly enlarged. No other pathological signs were detected on physical examination. A radiogram showed signs of chronic bronchitis and a few small densities in the neighbourhood of both the hilar regions. Blood picture: leucocytes 18,600, neutrophils 39, *eosinophils* 40, transitionals 4, lymphocytes 11, large monocytes 6 per cent. On the same day (29-6-43), the first dose of N A B, 0.15 gm, was given. On July 3, the leucocyte count was 12,500, neutrophils 38, *eosinophils* 26, basophils 1, transitionals 5, lymphocytes 25, large monocytes 5 per cent. N A B, 0.3 gm was injected. During the following three days patient felt such an improvement that on July 7, he took a heavy meal with plenty of beans to find out whether he still could provoke an asthmatic attack. The following night he felt only slight difficulty in breathing and wheezing appeared for a few minutes. The blood count, performed the next day (8-7-43), revealed some deterioration, viz., 15,000 leucocytes and 32 per cent *eosinophils*. No injection was given until July 7 because patient had to go on a short journey. However, having received only two doses of N A B, he felt perfectly comfortable, had a good, undisturbed sleep and the blood picture had considerably improved. The leucocyte count was 8,750, neutrophils 52, *eosinophils* 15, transitionals 4, lymphocytes 25 and large monocytes 4 per cent, the number of *eosinophils* had decreased from 7,440 per c mm to 1,300 per c mm. An injection of N A B, 0.45 gm was given. On July 23, the leucocyte count was 6,200, neutrophils 58, *eosinophils* 7, transitionals 4, lymphocytes 28, large monocytes 3 per cent. Patient was free from any complaint, exposed himself to all the factors which, only one month ago, according to his experience, regularly brought on an attack, without feeling now any bad after-effect, soap nut powder caused a short lasting irritation of the nasal mucosa but neither cough nor dyspnoea.

These two cases represent, apparently, different degrees of development of one and the same clinical syndrome, characterized by a mild bronchial asthma, leucocytosis, eosinophilia and prompt response to Novarsenobillon, whereas the radiological findings differ to some extent.

Differential Diagnosis One of the conditions, characterized by leucocytosis and eosinophilia of a degree, such as is found in our patients, is trichiniasis, this possibility can be excluded, the first patient being an orthodox Mohamedan who emphatically denied to ever have touched porc, whereas the other patient is a strict vegetarian. Other forms of helminthiasis have been excluded by repeatedly negative examinations of the motions. No skin disease was present in either of these patients.

Hodgkin's disease hardly ever shows a leucocyte count of more than 10,000 and rarely a considerable eosinophilia, certainly

not one of 50 per cent and more Equally out of place would be the diagnosis of a post-infective or post-toxic eosinophilia Excluded are also those cases of extreme eosinophilia, reported in malignant involvement of pleura or peritoneum, secondary to carcinoma of the ovary More difficult is the differentiation from allergic bronchial asthma Weingarten pointed out that the dyspnea is never so severe in the syndrome under discussion as it is in typical asthma cases and this holds good for our cases too, moreover, an uncomplicated case of bronchial asthma never has a high leucocytosis and hardly ever such a degree of eosinophilia

"Eosinophilic leukaemia," is, according to Price (1937) "not a disease entity and, certainly, not a real leukaemia but a syndrome of varied aetiology" which might develop as a peculiar reaction to bronchial asthma and bronchitis, malaria, hepatic cirrhosis, myeloid leukaemia Hodgkin's disease and syphilis In fact, Price finds anti-syphilitic treatment highly successful in such cases, if Wassermann reaction is positive This therapeutic effect, taken together with the text-book statement that eosinophilic leukaemia is characterized by a leucocyte count of 10,000 to 20,000, an eosinophilia of 20 to 80 per cent and a very good prognosis, makes it probable that tropical and leukaemic eosinophilia are overlapping syndromes It may be recalled that Weingarten discovered the effect of organic arsenicals upon the present syndrome when treating an eosinophilia patient for his co-existent syphilis Simeons (loc cit) uses the name "benign eosinophile leukaemia" for the condition under discussion

It remains to discuss the relationship of the present cases with Löffler's syndrome, a transitory lung infiltration associated with eosinophilia Having first described this condition in 1932, Löffler (1936) reported 57 cases of this kind Starting with fever of short duration and mild general symptoms, these patients develop a leucocytosis up to 15,000 and an eosinophilia of 10 to 50 per cent Sedimentation rate is usually 8 to 15 in one hour, sometimes more—Cough and signs of bronchitis are present, the sputum contains 20 to 60 per cent of eosinophils The radiological findings belong to one of the following groups (1) large irregularly outlined densities which are uni-or bilaterally localized, (2) small infraclavicular infiltrations such as described by Assmann, (3) multiple uni-or bilateral circular densities, (4) sharply defined densities in the right middle lobe, or (5) infiltrations, indistinguishable from the adult type of pulmonary tuberculosis A very peculiar feature of these cases was the extremely

transient character of the lung infiltrations which vanished spontaneously in three to eight days, whereas the eosinophilia frequently reached its peak when the radiological signs had disappeared. This short duration and spontaneous resorption of the lung infiltrations seems to permit for an easy differentiation from "tropical eosinophilia," although both the syndromes have got many features in common. However, Karan and Singer (1942) reported five cases from the U.S.A. which, as far as duration is concerned, form a connecting link between Löffler's syndrome and tropical eosinophilia, they lasted from a few weeks to several months.

Karan and Singer (*loc cit*) agree with Löffler that *aetiological*ly these cases are due to an allergic lung condition of an inflammatory character which Löffler compares with the manifestations of erythema nodosum and which he originally traced to ascariasis, although ascaris was not found in any of his cases. The comparison with erythema nodosum should not be misunderstood as an identification of these two conditions. Paul and Pohle (1941) examined radiologically lungs and mediastinum of twenty cases of erythema nodosum and found signs of hilum lymphadenopathy in a high percentage of them, pointing towards the tuberculous origin of this allergic manifestation, whereas the infiltrations associated with eosinophilia certainly have no connection with tuberculosis, although they are frequently mistaken for it (Karan and Singer, *loc cit*, Weingarten, *loc cit*).

The one feature which all the cases, seen by Weingarten and ourselves, have in common, is the fact that they fell ill some time after having stayed on the West coast or in a similar climate, as far as we know none of them developed symptoms and signs during the sojourn there. If such be the case, an allergic origin of this syndrome would become still more probable, every allergen needing at least some weeks to sensitize the organ which manifests the allergic state.

The excellent effect of organic arsenicals on complaints and blood condition could be explained by the assumption that these powerful disinfectants destroy the allergen producing agents, whether they be spirochaetes, spirillae, blastomycetes or other pathogenic organisms, all of them being very sensitive to these chemical compounds.

Pathologically, Weingarten's interpretation of the radiological findings as broncho-pneumonia or peribronchial infiltrations is acceptable also for our cases, the central translucence, visible

NON-TUBERCULAR PULMONARY INFILTRATIONS

By

Major J. R. OWEN

R A M C

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BOMBAY

1 THE EOSINOPHILIC LUNG

In the past twelve months *three* conditions of pulmonary infiltration have particularly attracted our attention. All our cases have occurred amongst soldiers, but there is abundant evidence that the general population is equally affected.

The *first* of these has some claim to be considered as a new disease entity, and for this the name of "Eosinophilic Lung" has been suggested.

Aetiologicaly, it is known to occur with some frequency in Bombay and to favour coastal or marshy districts, being found on the seaboards of Malabar, Coromandal, Gujarat, and Kathiawar. All ages and races, and the sexes equally are affected, the dietetic customs, habits and social or economic class appear to be without influence, nor does the disease appear to be infectious.

Clinically, the onset is insidious, with fever, lassitude and malaise, followed in a few days by the development of a troublesome and unproductive cough, which after a variable period becomes associated with bronchospasm and typical asthmatical attacks, usually nocturnal. The spleen now becomes enlarged to the extent of 2 or 3 finger breadths below the costal margin, and x-ray films show a fine mottling of broncho-pneumonic type in both lungs. A most striking and constant feature is the blood picture, which shows a leucocytosis consequent on an increase in the eosinophil cells.

In a case observed by us, the total count was 15,200, with 55% eosinophils, 28% neutrophils, 16% lymphocytes, and 1% monocytes. The highest count is recorded by Weingarten (*Lancet* 6230, Jan 23, 1943, 104), where in a total white cell count of 49,000, 89% were eosinophils, 10% lymphocytes and only 1% neutrophils. The sputum is scanty, mucopurulent, and tenacious, it contains eosinophils. The course of the disease is prolonged it may last for years, but no fatality has been so far recorded.

Diagnosis With regard to this, parasites have been diligently sought for in blood, urine, faeces and sputum with negative results

The syndrome, described by Loeffler, of transient pulmonary infiltration with leucocytosis and eosinophilia is dissimilar in that no such constitutional disturbances or asthma is present Infestation with trichinella spiralis may produce evanescent pulmonary changes with eosinophilia, but, in this disease, high fever, sweats, and pain with tenderness in the muscles and often dysphagia, dysarthria, and dyspnoea, serve to differentiate between the two conditions Filariasis may be regarded as excluded by the investigations previously referred to Other conditions in which eosinophilia may be associated with the radiological appearance of broncho-pneumonic mottling are myeloid leukaemia, polycythaemia and Hodgkin's disease In these, again, asthma is absent and the differential diagnosis readily made on clinical and haematological grounds

Treatment So strikingly successful is the administration of organic arsenical components that a therapeutic test is constituted Two or three injections of neoarsphenamine, acetylarsan, or metarsenobillon in doses slightly lower than those conventionally used in the treatment of syphilis are sufficient to abate the symptoms, and six injections to complete the cure There is evidence (Weingarten, vide supra) that the oral administration of the aromatic arsenical compounds such as stovarsol in a dosage of gr 8 daily is equally effective The success of these substances in therapy naturally raises the question of syphilis, but the disease does not resemble any known manifestation of that disorder, nor is the W R positive The credit for the first published account of this condition goes to Dr R J Weingarten, lately of Bombay and now Principal Medical Officer to Bikaner State

2 PULMONARY AMOEBIASIS

It is proposed to discuss next *pulmonary amoebiasis* due to the *entamoeba histolytica* The claim of this condition to be included amongst recent advances in knowledge is based on the recognition recently of certain features not previously noted

It is with the so-called primary type that we are chiefly concerned, in which the the cardinal symptoms are six in number

1 Cough, 2 Sputum, 3 Haemoptysis, 4 Loss of weight, 5 Night sweats, 6 Evening rise in temperature

The haemoptysis may give to the sputum the characteristic anchovy sauce appearance

On examination There is usually no clubbing of the fingers. Physical signs in the lungs consist of an area or areas usually in the mid or lower zones, with impaired resonance, diminished breath sounds and crepitations or moist rales.

Laboratory findings The diagnosis is suggested by the absence of tubercle bacilli from the sputum, the slight leucocytosis, with eosinophilia up to 10% and the presence of cyst forms of *E. histolytica* in the stools.

X-ray findings The affected areas may appear radiologically as a diffuse opacity, or as a mottling suggestive either of bronchopneumonia or of tuberculosis.

Treatment The usual remedies against amoebic dysentery are most effective, and, once more, may be regarded as a therapeutic test

Differential Diagnosis The conditions most likely to cause confusion are tuberculosis, bronchiectasis, neoplasm, syphilis, unresolved or atypical pneumonia, and a foreign body in a bronchus

The history and examination of the stools and sputum, W B C count, and response to treatment will in most cases serve to differentiate pulmonary amoebiasis. In suspected bronchial carcinoma, bronchiectasis, or foreign body, bronchography and bronchoscopy may be necessary to establish the diagnosis. Serial radiography will be of service to observe the response to treatment and distinguish amoebiasis from tuberculosis, unresolved pneumonia, and syphilis

Secondary pulmonary amoebiasis, is of course, by definition, due to direct spread through the diaphragm of infection from an amoebic abscess in the liver, and giving rise to infiltration, which may proceed to abscess formation, at the base of the right lung. Less frequently, right sided emphysema may be produced or the left lobe of the liver, left lung and pleura be affected. As far as I am aware no recent progress has been made in the diagnosis or treatment of this disorder, it is therefore not proposed to discuss it further

3 EPIDEMIC VIRUS PNEUMONIA

I would now like to call your attention to a condition of pulmonary infiltration which may occur in *epidemic form*. The description that follows is based partly on personal observation of two epidemics, and partly from the literature, which has re-

cently become considerable. A number of these cases I reported at a medical meeting held at the British Military Hospital, Colaba, early this year under the heading of "Atypical Pneumonia." Its characteristics are —

(1) Firstly, a rather abrupt onset of headache, fever and malaise without any marked catarrhal symptoms

(2) Transient and slight enlargement of lymphatic glands, most constantly the posterior cervical group

(3) The development after 2-3 days of a troublesome cough with scanty viscid mucopurulent sputum

(4) Variable fever up to 103° F with a relatively slow pulse, settling after five to fifteen days by lysis, sometimes showing a secondary rise

(5) The presence of an area, or areas, in one or both lungs of medium to coarse moist râles, accompanying breath sounds that may be either harsh or diminished

(6) The persistence of these signs, in some cases for many days after the disappearance of pyrexia

(7) Enlargement of the spleen up to 3 finger breadths below the costal margin

(8) An absence of any significant degree of leucocytosis with a tendency to lymphocytosis in the differential count and sometimes leucopenia

(9) A variable radiological picture, showing focal distribution, perihilar and peribronchial infiltration, broncho-pneumonic mottling which might become confluent, and in some cases areas of diffuse opacity

(10) Complete lack of response to treatment by sulphonamides including sulphathiazole

(11) The presence of a variable bacteriological flora in the sputum in the presence of an epidemic

Less constant features were orbital pain, photophobia, pain on ocular pressure, and two phase fever.

The severity of the condition was most variable—one case in sixteen died, while some ran a very mild course

A virus inspection of the lungs was suspected, and the Director of the Haffkine Institute, Col S S Sokhey, I.M.S., kindly consented to investigate this possibility. Experiments on mice, and attempts to grow a virus on the chorio-allantoic membrane of the chick embryo proved unsuccessful. I should like to take this opportunity of thanking Col Sokhey and Dr Rao, under whose ultimate direction these investigations were done

Exhaustive tests were also made to exclude tuberculosis, malaria, the enteric group of fevers, undulant fever, amœbiasis and septicæmia.

The researches at the Haffkine Institute were regarded as eliminating influenza, Q fever and psittacosis. Also, the onset was not that of influenza, and save in the fatal case, the disease was thought to be not severe enough for psittacosis but too severe for Q fever, which is stated in Manson's Tropical Diseases to be associated with a mortality of nil.

As mentioned previously, the literature abounds in the description of similar epidemics. In general, the features recorded are remarkably uniform and constant. All writers are struck by the absence of leucocytosis, the frequency of splenic enlargement and the lack of response to sulphonamides. In cases where post-mortem reports are available, the lesion appears as scattered areas of broncho-pneumonic consolidation. The bronchi may exude pus.

Histologically the interalveolar septa are thickened, and in the alveoli there is found an exudate consisting of many mononuclear cells, some red blood cells, and coagulated serum. Oedema is present, and the alveolar epithelium swollen. It will be noted that the nature of the alveolar exudate is quite unlike that seen in broncho-pneumonia caused by the common varieties of organism. In some cases, the cytoplasmic inclusion bodies suggestive of a virus infection have been found in the alveolar epithelium.

In the experimental investigation of the nature of the casual agent, pathological material has been introduced into all the common laboratory animals by every possible means and route. Most of these reports come from the United States. The only success was achieved by some working in Jamaica in the case of the mongoose, in which a pneumonia could be produced. Since this animal may not be imported into the United States, and since it is not in use as a laboratory animal in England, no further reports are available on the promising line of research, and it may be that we have the opportunity here in India to be first in the field.

TYPHUS FEVER IN BOMBAY

By

J. C. PATEL

M D (BOM), PH D, M R C P (LOND)

BOMBAY

Megaw (1917) described cases of typhus fever in India for the first time in 1917. A number of other workers, *e.g.* Covell (1936), Sharma (1940), T B Patel (1940) and Heilig (1940) have reported cases of typhus fever in various parts of India. T B Patel (1940) reported, while working in the Arthur Road Infectious Diseases Hospital, Bombay, 7 cases in April 1940 and further 15 cases in November 1940. These cases in Bombay were all admitted in the hospital as they were suspected clinically to be suffering from enteric fever. The temperature usually came down by about 10th to 16th day and it was found that all investigations, like blood culture and Widal reaction for enteric group of organisms, gave negative results, while Weil-Felix reaction was positive in increasing titres.

During the months of February to May 1943, among the cases admitted for continuous fever in the Singhanee Hindu Hospital, there were six cases which clinically resembled enteric fever but the temperature came to normal by lysis between 8th to 10th day of the fever. Bacteriologically they were not the cases of enteric group of fevers. Weil-Felix reaction was positive in all of them in very high dilutions. The common clinical features of these cases were as follows—In all of them fever began suddenly with chill, in few with rigor and was continuous for 8 to 14 days and came to normal by lysis in course of 2-3 days. All complained of intense headache, backache and severe aches all over the body but not joint pains. Some of them who came early to the hospital were apathetic and acutely ill and toxic with no other clinical signs, no hyperpyrexia or death, no rash or joint pains and no conjunctivitis. Lice were not noticed on the clothes. The other features are given in table No 1.

A paper read before the 28th meeting of the Seth G. S. Medical Staff Society, held on Saturday the 10th July, 1943, in the K. E. M. Hospital, Bombay, Dr N. D. Patel, M D (Lond) presiding.

TABLE I

Case no	Name	Age	Sex	Locality and Occupation	Onset & clinical features	Duration	Widal test	Malaria parasites	Total white blood cells per cmm	Ox 19	Ox 2	Weil Felix Reaction Ox K
I	A. N.	38	M	Curgaon Motor driver	Continuous fever for 6 days. Onset with rigor, severe headache, backache, toxic, slow pulse no other signs	14th day	Negative twice	Nil	4,400	1 1000	1 1000	Negative
II	S. M.	28	M	Tardeo Business	Continuous fever for 9 days severe headache, backache	14th day	Negative	Nil	14,850 17-4-43 21-4-43	1 125 1 500	1 50 1 250	Negative Negative
III	Y. T. N.	30	M	Curgaon Mill hand	Continuous fever for 10 days. Onset with rigor	12th day	Negative	Nil	7,500	1 1000	1 50	Negative
IV	P. S.	18	M	Tardeo Unemployed	Continuous fever for 8 days. Came to hospital febrile	8th day	Negative	Nil	8,000	1 1000	1 50	Negative
V	L. S.	20	M	Abdul Rahman Street Cooly	Continuous fever for 3 days headache	7th day	Negative	Nil	7,150	1 500	Negative	Negative
VI	J. S.	35	M	Mandvi Bhatia	Continuous fever with rigor, with headache for 4 days	9th day	Negative	Nil	11,500	1 500	Negative	Negative
VII	R. N.	30	M	Mazgaon Mill hand	Continuous fever for 4 days. Severe headache backache, sudden onset	14th day	Positive for O' in 1 125. Negative for 'H'	Nil	6,200	Negative	Negative	1 500

These cases clinically do not resemble typhus fever as described in the standard text books and as found in Central Europe and Russia. The only evidence on which they are taken as typhus fever is the positive Weil-Felix reaction in high titre, and in some cases there was increasing titre. Six cases agglutinated o x 19 strain, only one belonged to that of o x k. All the cases reported from Bombay by Patel (1940) were o x 19. Our cases came from different parts of Bombay round about Singhanee Hindu Hospital, Grant Road. There were no other cases from the same family but case No. V gave history that in the godowns where he lived and worked, there had been another case of fever about a month ago. From this one can infer that typhus is prevalent in various parts of Bombay and is sporadic rather than epidemic as compared to its outbreak in Europe.

These cases were noticed during the months of February to May 1943 in Bombay. Sharma (1940) has recorded that in Bangalore typhus fever has seasonal variations. He finds that it is present throughout the year but the highest incidence occurs during the months of March to July and it reaches another but smaller peak in the months of September to November. Sharma considers that this is due to variation in the humidity. When it is low with a high temperature the disease is prevalent. Bombay has a similar climate.

Covell (1936) drew attention to the presence of typhus infection in the wild rats of Simla hills, and considered that these rodents acted as reservoirs of the infectious agent for the spread of typhus fever round about the Simla Hills. Goyle (1941) also found infection of rickettsia in rats in Calcutta, and typhus fever has been reported now and then from the same city. T. B. Patel (1940, II) has suggested that rat flea might be the vector as there were no lice on the person of patients or their clothes. In the residence of some of the cases above reported, which were on the ground floor of a building, rats were supposed to be prevailing. It is quite possible that in these cases too rat flea might be an intermediate agent.

SUMMARY

Seven cases of continuous fever which resembled mild cases of enteric fever clinically but were negative bacteriologically and serologically but gave positive Weil-Felix reaction in high dilution are reported. These cases are taken as cases of a typical tropical typhus fever.

My thanks are due to Dr R. Row, Hon. Director, P. G. Singhanee Hindu Hospital for allowing me to report these cases and to the Director of Haffkine Institute for carrying out Weil-Felix reaction in all these cases.

DISCUSSION

Dr R G Dhayagude remarked that he was not prepared to accept the cases referred to by the lecturer as of typhus for the following reasons —(1) A non-specific agglutination test has been taken as a sole criterion for diagnosis. It is well known that agglutinins to the extent of giving a positive test in a serum dilution of 1:160 have occasionally been noticed when routine tests are done on Kahn sera. (2) Rash which is such a well known feature of typhus has been absent in every case. (3) Joint pains and conjunctivitis noticed in cases described by Heilig in Mysore were not observed in these cases. (4) Animal inoculation for Neill-Mooser reaction and for the detection of Pyrexia of Unknown Origin (PUO).

Whenever clinically atypical cases have to be dubbed as a particular disease entity one must be rigorous about the criteria for diagnosis, otherwise spurious cases will masquerade under that name. It is much better to say that they were undiagnosed than to give them a false label. Dr Dhayagude then gave a short description of the four types of typhus carried by vectors such as tick, mite, louse and flea and suggested that the most likely vectors to be looked for in Bombay cases, if they were of typhus, are the louse and the flea. Louse is concerned usually in epidemic typhus and in these sporadic cases the most likely intermediate host would be the fleas. An investigation of the fleas collected from rats found in the locality from which these patients came might throw some light on the etiology of these sporadic cases of fever which at present have to go under the omnibus label of Rickettsia were not carried out.

Dr N D Patel inquired if these cases were reported to the Bombay Health Officer. Dr Patel had seen a case last year which clinically appeared like typhus and where the Weil-Felix reaction was positive for $ox:19$ and $ox:k$ in 1:1000 dil. on the 8th and 15th day of the disease and was also positive after six months in 1:500 dilution for $ox:19$. This case was reported in the *Indian Physician*, (May 1942, p 231). The only atypical feature in this case was the rash, which was polymorphous—morbilliform rash, petechial haemorrhages, papules and vesicles which later became pustules. This was considered a result of large doses of quinine and sulfanilamide which the patient had taken before the case was seen by Dr Patel. A case of typhus was also reported by B R Patel, (*Indian Physician*, March 1942, Vol I, p 140) in a man of 27, who had come to Bombay from Mysore. The diagnosis was based on clinical grounds only. The Health Officer was asked about the presence of typhus in Bombay and he had answered that "11 cases of typhus were reported in 1941 and 3 in 1942. 13 out of these were reported by the combined Military Hospital, Colaba, and one by Col Bozman, Port Trust Health Officer, in an Italian prisoner of war sent out of Bombay directly from the ship. No definite information as to the exact vector was available in all these cases, except that lice or ticks which infested the jungle near the camp were suspected. These cases were not of typical text book type but probably a variety of Rickettsiosis. They showed the clinical signs and laboratory tests of

typhus" No cases were reported by the general practitioners or from the Arthur Road Hospital for infectious Diseases Dr Vengsarkar recently had informed the speaker that there were a few cases in the Arthur Road Hospital recently which had clinical features of typhus fever and gave a positive Weil-Felix reaction

The diagnosis of typhus fever should rest on clinical observation supported by laboratory tests—of the clinical features, apart from fever, rash is the most important sign It is said to be conspicuous in all cases of Louse or classical typhus, Tick typhus (Rocky mountain spotted fever or Indian Tick Typhus so well described by Megaw), and Mite typhus (Japanese River Fever), but it is inconspicuous or variable in cases of typhus of unknown vector described in literature as Tropical typhus, or Paratyphus of Kenya, Tunis, Marseilles or Brill's disease of New York Of the laboratory tests, leucocytosis and a positive Wilson-Weil-Felix reaction for *Proteus* o x 19 in high dilutions persisting for considerable time are present in all types—but these also may be variable in typhus of unknown origin and one has to rely only on clinical experience Neill-Mooser Test is a reliable test of Rickettsiosis and should be carried out if opportunity presents itself, to prove the presence of typhus in Bombay, though it is not invariably positive in all cases

Dr P Raghavan remarked that he must disagree with Dr Dhayagude and Dr Patel because in flea or murine typhus the rash has been described as absent or insignificant It is difficult to make it out in even fair complexioned individuals and much more so with our patients, the majority of whom are dark complexioned Though the Weil-Felix reaction is non-specific a high titre during the fever and rising titre during convalescence is diagnostic This short, indeterminate fever, which so far has been labelled Bombay fever, should be investigated from this point of view, because we have conditions here conducive to the presence and dissemination of typhus fever

Drs M J Shah and A. Hameed also took part in the discussion

Dr J C Patel, in reply to remarks from Dr N D Patel, said that these cases were reported to the Bombay Municipality, Health Department and they have been visited by the officials of the department in their homes The disease is probably in endemic form rather than epidemic form but these cases were noted only during these months (February to May) because of seasonal prevalence

With reference to the points raised by Prof Dhayagude it is true that in none of the cases rash, joint pains or conjunctivitis were noticed The speaker was aware of the four cases reported by Heilig in Bangalore which had atypical rash But from the same place Sharma has reported 56 cases of typhus fever in which he found rash in only 12 cases with fair skins All over the world Weil-Felix reaction is recognised as practically a specific agglutination test for the diagnosis of typhus fever, when it is positive in titre above 1 200 (Trop Dis Bull, February 1943, Vol 40, pages 130-131) If the titre is higher than 1 200 it is taken as evidence in favour of acute infection of typhus fever In these seven cases Weil-Felix reaction was positive in dilution of

1 500 or 1 1000 which was sufficiently high to consider them as typhus fever cases. This titre will not be anamnestic reaction because it will not be in such high and increasing titre, because, besides these seven cases, Weil-Felix reaction was done in five other cases of continuous fever (where anamnestic reaction could have developed) and found negative or positive only for 1 50 dilution on one examination. This became negative on repeating Weil-Felix test. So far there are no reports of agglutination tests done in India to find out in what titre the serum of an average normal person agglutinates the proteus strain of the organism. It would be an interesting research problem to investigate. As regards the injection of the blood of the patients in the guinea pigs to have an additional proof, we hope to undertake it in the Singhanee Hospital when some new cases are suspected of suffering from the disease.

Dr N D Patel, in concluding the discussion, remarked that the problem of typhus in Bombay was an important one. Our knowledge of the disease was very vague. Few had experience of its clinical manifestations. Laboratory investigations were meagre. Short fevers were dumped as Bombay Fever, Dengue, Influenza, and what not. The misuse of such medical terms had done enormous harm to medical progress and had vitiated medical statistical records. Louse or Epidemic Typhus was not present in Bombay but one could not rule out the presence of Sporadic Typhus where the vector was a tick, a flea, or a mite or some unknown insect, and where the reservoir was a rat, a mouse or a ground squirrel or some unknown animal. The problem was worth the attention of clinicians and laboratory workers. It will pay the investigator well, if in all short fevers where the diagnosis was doubtful, Wilson-Weil-Felix reaction in all cases as a routine, and the inoculation of guineapigs for Neill-Mooser-Scrotal reaction and the inoculation of rats, were carried out in suspected cases. The virulence of sporadic typhus was very variable and results of tests were also consequently very variable and the ultimate reliance must per necessity be put on clinical observation and record.

RECENT ADVANCES IN THERAPEUTICS

AS INDICATED BY THE TWELFTH 1942 EDITION OF THE
UNITED STATES PHARMACOPOEIA

By

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BOMBAY

(Continued from page 276)

The therapeutic usefulness of other members of the vitamin B group is not yet sufficiently established to warrant their inclusion in the new USP. It is, however, felt desirable to have available concentrated mixtures of the members of the B complex in appropriate proportion. A supplement to the USP, is, therefore to add a tablet and a capsule each containing the *mixed vitamins* of 250 mgm of Liver Extract fortified with Thiamine, Riboflavin, Nicotinamide, Calc Pantothenate and Pyridoxine. There is also to be a similar powder of liver extract for oral administration and a similar material in liquid form for parenteral administration.

For the prophylaxis and treatment of scurvy and other vitamin C deficiencies, the USP includes *ascorbic acid*, which was added to the BP by the 1st addendum, and its tablets. Its average daily dose established by an extensive experience, for oral administration is 50 mgm.

DIAGNOSTIC AGENTS

Two dyes used for function tests have been added to the USP. *Sulfbromophthalein* Solution is used for the determination of liver function. The normal liver excretes most of the dye within 30 minutes. The solution is injected intravenously and 30 minutes later a sample of blood is drawn and the dye content of the alkalinised serum is determined colorimetrically. Another dye added is *Pheno-sulfonphthalein*. It is used for testing the renal function. Six mgms of the dye are given by intramuscular or intravenous injection, the urine is collected over suitable intervals, and the dye content of the urine is determined colorimetrically. Normal kidney excretes approximately, after intravenous injection, 50-60% of the dose in 30 minutes and 65-80% in 60 minutes, after intramuscular injection, 60-80% in 120 minutes. Since some of it is excreted by the bile, supranormal values are suggestive of hepatic insufficiency.

ANTISEPTICS

It is not known why *sodium sulfite* has been added to the USP. It is sold under various names, such as "meat preserver" or "preserv-

ing salt," and these names probably show its use. Rost has found that it is not harmful in the concentrations (0.4-2%) used as preservative, because it is nearly completely oxidised to sulphate in the body. It is used to preserve food, beverages and to improve the appearance of foodstuffs. It is said even to improve the odour and appearance of spoiled meat. That is why its use to preserve meat and meat foods is prohibited by law in many countries. Some authorities, however, do not consider it so harmless. *Pyrogallol* is not much used as an antiseptic in therapeutics and has, therefore, been deleted. Although it possesses significant fungicidal properties, its toxic properties preclude its wide use in skin infections. *Iodoform* has also been omitted because it is "vile smelling and of low rating as an antiseptic." It is now being replaced by more effective agents which do not possess the disagreeable odour. *Acridine* was employed extensively in the last world war, but since then its use in the U.S.A. has steadily declined. It is bacteriostatic rather than bactericidal. The sub-committee of the Nat. Res. Council in America has repudiated it on the ground that it is ineffective in the treatment of wounds and this substance and its hydrochloride salt have now been deleted from the U.S.P. Although *Acridine* is the most employed member of the acridine group, it is the least satisfactory. *Proflavine* which has been added to the B.P. by the 4th Addendum is far superior to it. It is an efficient wound prophylactic and in the prevention of gas gangrene it is said to be even superior to sulphonamides. *Dichloramine-T* and *Dakin's solution* have also been omitted from the new U.S.P. on the ground of their inefficiency, but the water soluble chloramine-T has been retained. *Dakin's* hypochlorite solution has also been deleted and for the slow and steady liberation of chlorine, *azochloramide* (chlorazodine) is considered superior. It is claimed that this compound has a higher bactericidal activity in the presence of organic matter, and it is said to be less irritating and less toxic than the hypochlorites, therefore this substance and its solution have been added to the U.S.P. Potassium *chlorate* was introduced as an oxidising germicide but was found to have little more action against bacteria than inert salts, on the other hand, it is likely to cause systemic poisoning. Therefore, it has been omitted from the U.S.P. on the ground that "it is an antiquated mouth astringent and any internal use for it is not justified." *Terebene* which has been administered by mouth or by inhalation as an "expectorant" and mild antiseptic, particularly in chronic cough has been deleted, because it is stated to be "neither antiseptic in the respiratory tract nor valuable as an expectorant." The same reasons are given for the removal of *creosote* and *guaiacol* and their relatives (creosote carb and calc creosotate). No evidence exists to support the use of these drugs in pulmonary infection by tubercle bacilli.

* Editorial, B. M. J. 1943, I, 355

† Chloramine T and dichloramine T are derivatives of p-toluene sulphonamide and an interesting fact is that these were the only members of the sulphonamide group widely used in medicine, till the introduction of sulphamidamide and its derivatives as chemotherapeutic agents.

When administered orally they are mainly excreted in the urine. Creosote has also been employed by inhalation for its "expectorant" action in chronic stages of bronchitis and bronchiectasis. The sputum is then less objectionable in taste and odour. The bactericidal potency of creosote is, in general, about 2—3 times that of phenol. But the local antiseptic value of creosote, especially when introduced into the tooth cavity, and its deodorising value were not considered sufficient for its retention in the USP.

Some Balsams, including balsam of copaiba are also, similarly, employed as antiseptic expectorants, but copabia balsam has been more commonly employed as a urinary antiseptic. Sandalwood oil has also been similarly in use as a urinary antiseptic. Both are irritant to the stomach and may irritate the kidneys, while they are not effective antiseptics of the urinary tract. They are much inferior to the modern urinary antiseptics. The balsams contain benzoic acid and its esters. Benzoic acid has been sometimes used as an antiseptic and widely used as a food preservative. Sodium benzoate has been credited with some virtues as an intestinal and urinary antiseptic. Ammonium benzoate has been given to acidify urine but it is not as useful as ammonium chloride or acid sodium phosphate. Ammonium benzoate was also used as a substitute of sodium benzoate on the fallacious belief that the ammonium-ion was in some way protective to the heart. It has now been deleted from the USP. Similarly, ammonium salicylate which has no advantages over sodium salicylate has also been removed from the USP. One recent effective urinary antiseptic is mandelic acid which was already admitted to the USP and was added to the B.P. by the 4th Addendum. When mandelic acid is administered, it is neutralised with sodium bicarbonate, but then an acidifying agent such as ammonium chloride has to be given in order to assure a proper degree of urinary acidity, i.e. below pH 5.6, because mandelic acid is only active in acid urine. More acidic the urine, the more bactericidal it is. It was shown that 0.25% mandelic acid was bactericidal at pH 5, while 1% at pH 5.7. Sodium, ammonium and calcium salts of mandelic acid are now available, but if the sodium salt is prescribed, it should again be associated with an acidifying agent. But the treatment is simplified by the use of ammonium and calcium salts which are both in themselves acidifiers due to the change of ammonium into urea and retention of calcium in the intestine, as calcium carbonate, or in the bones. Therefore, ammonium mandalate (in the form of a syrup) and calcium mandalate are now added to the new USP. Mandelic acid is particularly effective against *B. coli* but, since it requires acid reaction, it is not effective against bacteria which cause ammonia formation from urea and thus make the urine alkaline. Acid urine is also irritant to the inflamed mucous membrane and causes pain, especially in the acute stage. Sulphonamides act well in alkaline and acid urines, hence adjustment of urine reaction is unnecessary. Limitation of fluid intake is also not necessary in sulphonamide therapy, which has been found to be very efficacious in urinary in-

fections, also in cases of *B coli* infections. The relative value of the sulphonamide drugs now added to the USP is discussed below. *Hexyl resorcinol* which is non-irritant to the urinary tract, was recommended as a genito-urinary disinfectant in 1924, its activity not being influenced by the reaction of the urine. But much of the excited portion is in a conjugated form which greatly impedes its action. It is less efficient than mandelic acid, sulphonamides and hexamine.

ANTHELMINTHICS

Hexylresorcinol was developed as an anthelmintic in 1931, and has now been admitted to the USP. It is perhaps the most valuable single anthelmintic agent, being effective against hookworm, ascariis, oxyuris, dwarf tapeworm and whipworm. Although it may not be the most powerful, its range of activity makes it suitable in mixed infestations. Its toxicity is low and so it can be repeated. It is particularly useful when more specific anthelmintics may be contraindicated. It is reported to be effective in removing round worms (90 to 100% efficient), hookworms (75-85% efficient), and also whipworms (40-45% efficient). It is given in the morning on an empty stomach in capsules, in doses ranging from 0.5 to 1 G (regardless of the parasite to be treated) followed by a saline purge after a couple of hours. Food may be eaten after 5 hours have elapsed. The drug may be repeated at 3 day intervals. Enemas containing hexyl resorcinol were found to be efficacious against threadworms, but better results are claimed from the oral administration of gentian violet. It may be added here that Diphenan (oxylan, butolan) or p-benzyl-phenyl-carbamate which is also used orally (as tablets), in threadworm infection has now been included in the 3rd suppl to the BPC. It is also said to be of value in trichiniasis. The latest addition to the threadworm remedies is phenothiazine or thiodiphenylamine. Newer remedies like hexylresorcinol and chenopodium oil, have now taken the place of *santonin* which has now been deleted from the new USP. The routine drug of choice for the treatment of hookworm infections is *tetrachlorethylene* because of its low toxicity and relatively high efficiency. It has now been added to the USP. Its action is similar to that of carbon tetrachloride but it is absorbed less readily owing to its low solubility in water and hence its toxicity is much lower. No fats, oils or spirits are to be taken with it or soon after. Doses of 15 minims are given in capsules, 1 capsule every hour for 4-5 hours, followed by a saline purge.

CHEMOTHERAPY

In the new USP, there has been a reduction in the number of *mercury compounds* used for the treatment of syphilis. *Yellow mercurous iodide* has been deleted, because it has been supplanted by more desirable remedies. It was formerly administered as an oral antisyphilitic. Oral doses are no longer provided also for mercury bichloride and mercury succinimide. Thus, the only preparation for

oral use for antiluetic therapy now left is the grey powder (mercury with chalk). Standards for official injections of mercuric salicylate and mercuric succinimide have been provided as well as those for injections of *Bismuth* and potassium tartrate and for bismuth sub-salicylate.

A number of organic arsenical compounds have been added to the new U.S.P. but it is a question whether the newer compounds have brought about any significant improvement in the treatment of syphilis. Sulpharsphenamine, which is suitable for intramuscular injection has been added to the new U.S.P. It is already included in the B.P. Tryparsamide, a pentavalent arsenical suitable for the treatment of neurosyphilis and African sleeping sickness, has also been added. It was added to the B.P. by the 1st Addendum. The third compound added is *Bismuth sulpharsphenamine* (Bismarsen). It represents a combined arsenic and bismuth therapy in one compound for intramuscular injection. Like sulpharsphenamine, it is another compound for intramuscular administration and when it is properly injected, immediate reactions appear to be fewer after its use. But it is not as effective as the other arsphenamine compounds. Therefore, it is not suitable for routine therapy but it may be reserved for cases in which intravenous therapy with the better known arsenicals is not possible. The presence of Bismuth in the compound is contrary to the present-day conception of alternating the courses of arsenic and bismuth (or mercury) and with its use, one has to be on the alert for symptoms of bismuth as well as of arsenical poisoning. It is feared that the simultaneous use of arsenic and bismuth for a long period is likely to increase the chance of producing drug-fast strains of trepanomes.

Another organic arsenical added is *metarsen* (mapharsen) or the hydrochloride of arsenoxide. It represents a partial oxidation product of arsphenamine and has a direct spirochaetocidal action. It appears to be superior to neoarsphenamine and is believed by some to be the substance by means of which arsphenamines act. It has received extensive trials and there are abundant reports in its favour. It appears to be one of the most promising trepanemicidal arsenicals. It gives neutral solutions, not colloidal, and so the reactions due to these physical properties are absent. It is given by intravenous injection. Irritation of the vein is one disadvantage but it can be lessened by rapid injection.

Since the main sources of supply of quinine have now been cut off, attention has been directed in America to the use of other alkaloids of cinchona as antimalarial agents, with the result that alkaloidal mixtures from cinchona, even relatively poor in quinine, have been found to be nearly, if not quite, as effective antimalarials as quinine itself. It may be added here that the Indian Government mixture, called cinchona febrifuge, was of inconstant composition and contained practically little or no quinine. *Totaquine* a mixture of constant composition has already been included in the B.P. and the mixture contains not less than 70% of crystallisable alkaloids of

which not less than one-fifth is quinine. It had been recommended by the Health Committee of the League of Nations for reducing the cost of combating malaria. Totaquine has now been admitted to the USP, but the standard adopted for it is such as to conform to the average composition of the alkaloidal mixtures obtained from Central and South American sources. These sources now available have a rather low content of quinine and so Totaquine (USP) is to contain at least 7% of quinine. It is to be used in doses of 10 grains three times daily. Quinine (base) and Tinct cinchona are deleted from the USP but quinine hydrochloride is admitted. Particularly, the solution of quinine hydrochloride is included for use as a sclerosing solution.

The adoption of totaquine as a substitute for quinine is not sufficient to meet the serious shortage of quinine, and hence *Quinacrine* (atebrine) the synthetic antimalarial remedy, an acridine dye, as well as its tablets, has been admitted to the USP. It was already added to the BP by the 3rd Addendum under the name Mepacrine. It is unfortunate that identical name has not been accepted by the two pharmacopoeas in English. Like quinine, quinacrine is chiefly effective against the asexual forms of malaria parasites. The pharmacopoeic dose is 0.1 taken thrice daily for 5 days, its toxicity, after oral administration, is low, but it has a tendency to accumulate and in a considerable number of cases it produces a distinct yellow tinge in the skin. Therefore, an interval of a month or two is often allowed to elapse before the course is repeated. It does not exert an oxytocic action. The question of the relative efficiency of quinine and this drug and of the choice of drug under specific circumstances is not yet settled. According to the Malaria Commission of the League of Nations, there is no preference except one of expense, but this question does not arise now when quinine is scarce. Pamaquine, which is the name given to plasmoquine (or plasmochin) in the 4th Addendum to the BP is another synthetic antimalarial agent, but it acts against gametocytes and thus makes the blood non-infective to mosquitoes. It has much less effect on the asexual forms of malaria parasites which cause clinical symptoms. Therefore it is only important in preventing the transmission of malaria from one person to another. It has not been included in the USP.

Two substances used in the treatment of amoebiasis have now been admitted to the USP. They are not meant as substitutes for emetine, but have their own special fields of usefulness in the treatment of the disease. Amoebiasis is essentially an infection of the large intestine with systemic invasion. The parasites are present in the intestinal contents, in the wall of the intestine and in the tissues of the host, particularly in the liver. Emetine, the old remedy which is administered parenterally is particularly useful in eradicating the amoebae in the tissues, in cases of hepatitis and amoebic abscess of the liver. But it has little effect on the amoebae present in the intestinal lumen, and therefore it is of little value in the treatment of carriers. Used alone, it can, therefore, cure the disease in only a

small proportion of cases of amoebic dysentery. In the form of emetine-bismuth-iodide, emetine can be administered orally and this compound is said to be a more powerful amoebicide. The iodine content probably accounts for it or it may be the oral route which enables the unabsorbed drug to reach the large intestine. But it is also not as effective clinically as the newer drugs. The two classes of substances now used mostly orally to supplement the effects of emetine are arsenical compounds and halogenated quinoline compounds. Acetarsol (stovarsol, acetarson) is the arsenical in the B.P. used in the treatment of amoebic dysentery, but carbarsone which is now added to the U.S.P., is preferred because it is less toxic and more efficient. Acetarsol has only $1/8$ the therapeutic index of carbarsone. Carbarsone is administered orally in capsules and it attacks the organisms in all their locations i.e. in the intestine as well as in the tissues. It is, therefore, useful in carriers. Its U.S.P. dose is 3 grains. It is given thrice daily for 10 days. It is absorbed and slowly excreted and, therefore, an interval of, at least, two weeks must elapse before the course is repeated. The free forms are stated to be more easily eradicated by rectal administration of 2 G. in 200 cc. of a 2% solution of sodium bicarbonate (because it is soluble in alkalis) every other day. After therapeutic doses usually no toxic effects are observed, but when they occur, they are the same as with other arsenicals. A possible toxic effect upon the optic nerve should be kept in mind. *Chiniofon* (yatren) which is now admitted to the U.S.P., is a halogenated quinoline compound. It was added to the B.P. by the 1st Addendum. It is used orally or as retention enema. It dissolves in water with effervescence. Its toxicity is low, because little is absorbed, but occasionally, enough may be absorbed to injure the liver. It is however, irritant to the gastro-intestinal tract and may cause diarrhoea. But some people consider a moderate hyperperistalsis with diarrhoea as a distinct aid in washing out the amoebae. In view of the limited absorption, it has little action in the tissues. It is useful chiefly for the eradication of the parasites within the intestinal lumen.

Since the time of Ehrlich, great advances had been made in chemotherapy of protozoal and metazoal diseases but the problem of bacterial diseases remained unsolved until the discovery, in 1935, of the effectiveness of the original prontosil in the treatment of streptococcal and staphylococcal infections. During the intervening period, attempts were made to discover specific remedies against bacteria with the result that *Ethyl-hydrocupreme hydrochloride* (optochin), a derivative of quinine, was introduced for the treatment of pneumonia. It was found to have a remarkable selective action on pneumococci in vitro. Moreover, it was found possible to inject quantities of the substance sufficient to render the blood of experimental animals bactericidal, but such doses did not protect them against lethal doses of pneumococci. Clinically, it proved too toxic for oral and parenteral use and ineffective in pneumonia or systemic pneumococcal infections. It was found to cause blindness, and deaths

resulted from its intravenous use. But it has been applied locally (as ointment or 1-2% solution) in pneumococcal infections of the eye or in stomatitis in infants. For this use, it is now supplanted by the sulphonamides and has been deleted from the USP.

The original prontosil dyes were found to yield in the body the colorless substance, p-aminobenzene sulphonamide, which unlike prontosil, was effective against bacteria in vitro and was even more effective than prontosil, in curing experimental infections in animals. Thus, this simple and less toxic substance supplanted the prontosil dyes and came into general use. The Am Med Assoc gave it the name "*Sulfanilamide*" and this name has been generally adopted (although, according to Ardley, it is sold, at least, under 42 different names). It has been taken up in the 4th Addendum to the B P and also in the new USP. Its use was extended to therapy of infections other than those due to haemolytic streptococci. But, researches were carried out with the object of obtaining more effective and less toxic drugs and of widening the scope of effective treatment of infections in which sulphanilamide had failed. More potent derivatives of sulphanilamide have been obtained. Sulphanilamide, as well as its derivatives, contains the sulphonamide group ($-\text{SO}_2\text{NH}_2$) and so the generic name sulphonamide has been given to the whole class of compounds. It is not the name of any one compound. Three of these derivatives have been included in the 3rd supplement to the BPC viz, sulphacetamide (albucid), sulphapyridine and sulphathiazole. The last two are admitted to the new USP. *Sulphapyridine* ("M & B 693," Dagenan) introduced in 1938, extended chemotherapy by bringing pneumococcal infections within its scope. It has had clinical trials in almost every disease, for which sulphanilamide has been employed and can be used in any of the conditions for which the latter is indicated, but in view of its greater toxicity, it is safe not to employ it in preference to sulphanilamide, unless and until the results with it have been proved to be better. It is almost equally good for streptococcal diseases but in gonorrhoea, in meningococcal infections and in gas gangrene it is more effective than sulphanilamide. *Sulphathiazole* ("M & B 760") synthesised in 1939, has the special advantage of greater effect in staphylococcal infections in which it is particularly indicated. It seems to have an advantage over sulphapyridine in infections due to clostridia, *Pasteurella* (plague) and Gram negative enteric bacilli. It is difficult to dogmatise about the relative merits of the sulphonamides. One important factor, in the choice of the drug, is the relative efficiency of the drug in the particular infection to be treated. Other things being equal, there is no indication for the use of any but the strongest drug against the infecting organism. In general, sulphanilamide is less potent than its derivatives, except perhaps against group A haemolytic streptococcus. But its high diffusibility and lack of toxicity for the kidney are assets which outweigh its drawbacks. It is also useful for subcutaneous and intrathecal administration, and so may be employed to initiate therapy in meningitis. Sulphathia-

zole is potent in small doses against the common organisms causing urinary infections. It is rapidly excreted in the urine in high concentrations and hence, gives best results on the smallest dose. The following table adapted from Janeway* summarises the dosages and other information connected with the use of this drug.

Table of Dosage Schedule for average 150 lbs adult

Drug	Initial dose G	Maintenance dose G	Desired blood level mgm %cc	Fluid in take cc	Desired urine output cc/24 hrs	Dosage of Sod Bicarb
Oral administration —						
Regular dosage for general infections						
S'nilamide	4 0	1 to 1 5 every 4 hrs	8 15	restrict	1500	equal amount
S'pyridine	4 0	1 every 4 hrs	5 10	Force	2000	none
S'thiazole	5 0	1 1 5 every 4 hrs	3 5	"	2000	"
Gonorrhoea, unless septic complications exist						
S thiazole	3 0	0 5 4 i d	—	—	1500	none
Urinary tract infection, unless very severe						
S thiazole	—	0 5 4 i d	—	Force	2000	may be used to keep urine alkaline, the drug being effective in alkaline medium

Both sulphapyridine and sulphathiazole are being extensively used in bacillary dysentery but they are likely to be supplanted by newer derivatives like sulphaguanidine and succinyl-sulphathiazole. Toxic reactions may follow the use of these sulphonamides to a greater or less degree. It would, therefore, be wrong to give such drugs without specific indications, but it would be equally wrong to deprive a patient of their benefits where he is seriously ill. Infections due to organisms susceptible to these drugs should be treated with them only if they are severe or spreading. In general, sulphonamide therapy is more successful in acute than chronic infections. Localised infections associated with accumulation of pus are resistant to these drugs but they are very effective in aiding the localisation of spreading infections. If the pus can be removed, the sulphonamides then assist the cure. Sulphonamides are, however, employed locally on wounds, burns, skin diseases and in contaminated peritoneal and pleural cavities, as antiseptics.

IMMUNOTHERAPY

It is now clear that high degree of immunity to tetanus can be obtained by the prophylactic use of *tetanus toxoid* which has been added to the BP by the 2nd Addendum and also included in the new U.S.P. A protected individual, nevertheless, if subject to extensive and dirty wounds, cannot dispense with the antiserum and a prophylactic dose of the serum should be administered to such an individual.

* Janeway, C. A. New Engl J Med 24 & 31 Dec 1942 p 989 & 1029

Human scarlet fever immune serum, convalescent serum, has been added to the U S P, but it may be said to be on its trial and no definite statement can be made as to its value. Similarly, *human measles immune serum* has also been added. It is stated that a convalescent serum obtained within three weeks of the fall of temperature to normal will, if injected intramuscularly, produce complete but temporary immunity in about 70% of cases. The remainder, who develop measles, have it very slight. This is the value of the serum as a prophylactic agent. Another preparation, useful in the prevention of measles, admitted to the U S P is (*human*) *immune globulin*. It is a preparation of globulin obtained from human placental blood containing immune factors against measles. It is equivalent in usefulness to the convalescent serum. Injected intramuscularly, in the early days of the incubation period, it may protect the contact from the attack. Usually, however, it merely modifies the disease.

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I have not been able to secure a copy of the U S P XII or a copy of the 3rd Supplement to the B P C. This review is therefore mainly based on the publications mentioned below —

Editorials J A M A 14 Dec 1940, p 2087 and 6 Dec 1941, p 862

Cook, I F J A M A 6 Dec 1941, p 883

Gold, H and Iggleston C Am J Med Sc May and Nov 1942, pp 759 and 757 respectively

Editorial notes Pharmaceut JI 27 Sept 1941, p 116 and 21 March, 1942, p 107

Annotation Lancet, 18 April, 1942

Besides the books on Pharmacology by Cushing (1941), Clark (1940), Goodman and Gilman (1940) Davison (1940) and Hale White's *Materia Medica* (1942), the following have been consulted —

Bull Hdbk of Nutrition, XI, Fat Soluble Vitamins J A M A, 28 Nov 1942, p 1030

Elvehjem C A Hdbk of Nutrition, XI, Water Soluble Vitamins, J A M A, 26 Dec 1942, p 1388

Jancray New Eng JI Med 24 and 31 Dec 1942, pp 989 and 1029

CORRIGENDUM P 268, lines 15-16 The sentence should read

"in a chick a rat unit of vitamin D₃ is nearly 20 times as effective as that of vitamin D₂."

Critical Notes and Abstracts

ALLERGIC BRONCHITIS WITH EOSINOPHILIA

That certain atypical forms of asthma, especially in younger subjects and of short duration, respond favourably to intravenous neosalvarsan or intramuscular arsenicals, is well known to many practitioners in Bombay. In fact that is the stock treatment used by the so-called asthma specialists of Bombay. The presence of leucocytosis and marked eosinophilia, especially in those cases which respond well to arsenicals, and the association of periodical bouts of fever are also well known to many physicians. The writer must have treated scores of such cases during the last twelve years in Bombay. Of the few recent cases the eosinophil counts were as follows

No	Name	Age	Total white cells	N	E	B	L	LM%
1	B L	24	43,680 per c mm	9	79	—	10	2
2	V S	25	17,650	30	42	—	28	—
3	V L	30	32,780	39	51	—	0	1
4	D V	20	30,000	24	44	—	31	1
5	N Y	27	10,300	44	25	—	28	5

The significance of high leucocyte and eosinophil count is not understood, though it is taken as a sign of allergic reaction. In differential diagnosis of bronchitic states, Naegeli has stated that *"periodic bronchitis very strongly speaks for asthmoid states, usually of the mild type which has been designated as eosinophil catarrh"*. Haematologic changes may indicate the nature of bronchitis. First of all one should think here of eosinophilia in all allergic and asthmatic states. Allergic, anaphylactic processes today are often considered to be the cause of pulmonary infiltrates, especially fleeting eosinophilic infiltrates" (O Naegeli, Differential Diagnosis in Internal Medicine, 1940, pp 363, 368,) *"Pulmonary infiltrates with eosinophilia. This disease does not seem to be at all rare. It is one with ephemeral infiltrates equally distributed through the seasons, with slight clinical findings, slight impairment of resonance, a few rales, and moderate fever. It is variously localised in the lung, both in the upper and lower lobes. Roentgenologically the foci are mottled. There is moderate leucocytosis. The temperature is moderate and seldom and only for a short time above 102° F. Blood eosinophilia is quite striking and may last for some time. Sputum need not always be present, but if so it is purulent and without any characteristic features and does not contain tubercle bacilli or pneumococci, even after persistent examinations"* (O Naegeli, pp 373-4)

The writer has learnt to divide his cases in three groups

(1) *The acute cases*, where there is a more or less continuous fever with spasmodic bronchitis. The spasms are very like those of whooping cough. The blood shows eosinophilia and leucocytosis. The general condition of the patient is relatively good and the pulse-rate relatively slow. The x-ray picture shows diffuse gene-

ralised infiltration which is similar to the picture seen in miliary tuberculosis, silicosis, or congestive cardiac failure The recovery is complete in most cases

(2) *The subacute or chronic cases* These cases go about under a variety of different labels, such as atypical asthma, chronic bronchitis, pulmonary tuberculosis, or chronic bronchopneumonia The eosinophilla is variable and the x-rays show various types of infiltrates, peribronchial and hilar areas being the commonest affected Bouts of fever, cough, loss of weight together with the x-ray appearance make the diagnosis of chronic lung tuberculosis irresistible Some of these cases make a spontaneous recovery, some respond strikingly to intravenous arsenicals, while others deteriorate steadily in spite of all treatment, and make up the third group

(3) *Chronic cases with ultimate pulmonary and cardiac failure* With passage of years the patients develop marked emphysema, and fibrosis of the lungs The asthmatic attacks give way to more or less continuous dyspnoea The eosinophilla is not present now There may be bouts of fever with leucocytosis and patches of bronchopneumonia The patients usually die in early forties from congestive cardiac failure or from some terminal infection

It has been suggested that the disease is peculiar to the Western coast From the above description of the disease given by Naegeli who practised in Zurich, and also from my experience, it appears to be prevalent also in dry inland places The following case, under observation with me at present, will illustrate this

Case Report

S S, a policeman, aged 35, has lived all his life in Buldana, a district in Central Provinces, and has come to Bombay for the first time for treatment He had never left his district and never lived on the sea coast There is no family history of allergic diseases The history is that for the last two years he is being troubled with cough, without expectoration, irregular fever, loss of weight, vague abdominal pains and vomiting soon after food Paroxysms of cough and breathlessness with wheezing are the most troublesome The physical examination showed only rhonchi over both sides of chest and evidence of loss of weight, his usual weight of 142 lbs has come down to 112 lbs The sputum, the urine and the stool examinations are negative The x-ray examination shows diffuse infiltration spreading out from both hilar areas and there is much peribronchial basal fibrosis The following is the record of his blood examinations

Date		Total W B C	PV	E	B	L	LM %
18	August 1913	7,000	30	35	—	22	4
20	" " "	9,350	30	40	—	30	—
23	" " " N A B	0 15 G					
25	" " "	6,500	40	40	—	10	1
27	" " "	—	30	57	—	12	1
30	" " " N A B	0 30 G					
1	September "	7,000	44	31	—	22	3
7	" " " N A B	0 45 G					

N. D. P.

HIDRADENITIS SUPPURATIVA

Recently two cases have been under my care, one of chronic suppuration in the axillae and the other of chronic suppuration in the perineum, which fit in with the condition described in the literature as *Hidradenitis suppurativa*. Most practitioners are not familiar with condition and a variety of false diagnosis are made. A brief description of these cases, and a short resume of Brunsting's articles about it, will not be out of place here.

Case 1 Mrs R, a Hindu, strictly vegetarian, healthy robust woman of 24, very obese (weight about 170 lbs for the height of 64 inches), had multiple abscesses in the perineum. These began as indolent swellings which suppurated in time, some healed on their own but new ones were formed from time to time. Ultimately the condition became so troublesome that she had to stay in bed. When I saw her she was practically in bed for nine months. On examination of the perineum, there were seen some six perianal abscesses on the left side and three on the right side. The sinus tracts were not deep, only in one the probe could go upto about an inch, the others were quite superficial. Besides the open abscesses, there were a few indolent swellings. There were no swellings in the axillae or elsewhere in the body. There were no physical signs of any disease in the lungs, the heart, or the abdomen. She gave a history of gonorrhoea and the blood Kahn was four plus. The husband gave a similar history of venereal infection. Several surgeons had seen her and advised her to have the sinuses treated surgically but she had flatly refused to have surgical help. The diagnosis of *hidradenitis suppurativa* was made and she was put on sulphathiazole by mouth and a sulphathiazole powder and an ointment for local application. Within five days there was a surprising change in the appearances of the abscesses and the patient thought they were more than half cured. After a further use of local sulphathiazole for five days, the discharge had disappeared, and the granulations looked so healthy that an occlusive dressing of elastoplast was applied on both sides and she was advised to move about in the house and even go out of the house if she liked. The elastoplast was changed every five days. Within a month the abscesses on the right side had completely healed and within the next two months the abscesses and the sinuses on the left had also disappeared. She was given a course of eight N A B and twelve bismuth injects during this time.

Case 2 Miss I, a Parsi girl of 16, was recently seen by me, suffering from multiple abscesses and sinuses in both axillae for the last 2½ years. She was a well-built, well nourished, healthy, robust girl. The history was that some two and a half years ago, the trouble started with itching in one axilla. After a few days an indolent swelling was observed which was fomented. A doctor who saw it incised it and some thick cheesy pus was evacuated. Four months later a similar swelling appeared on the other side which also was incised. After this several indolent swellings appeared on both sides adjacent to the original lesions. These were treated with fomentations and ointments. A surgeon who saw her at this time advised conservative treatment and ointments were continued for the next six months. By this time there were many discharging sinuses and she had much pruritis, discomfort, and pain. A year and a half ago,

January 1942, the surgeon decided to operate and a radical operation for the excision of glands in both axillae was carried out. But the wounds did not heal and the sinuses persisted in spite of all local treatment. When seen by me, June 1943, she had several sinus tracts and multiple small subcutaneous swellings, forming typical chord like elevated bands, in both axillae. A diagnosis of hidradenitis suppurativa was made and she was put on a five per cent cibazole ointment and cibazole tablets by mouth. In a fortnight there was considerable local improvement. After a further period of two weeks with local cibazole application, it was discontinued and an occlusive elastoplast dressing was applied in the first week of July. After three applications most of the sinuses had healed, local pain and itching had disappeared and she felt fit enough to make social calls and even attend dances without any dressing. But still a few small swellings persisted or reappeared and from a point or two on either side, a bead of pus could be expressed. As she had developed a few acne spots on both cheeks, *acne conglobata* was thought of and following Sutton and Mark, she was put on a complete fat free diet and thyroid extract by mouth. By the end of the week she showed surprising improvement and by the end of the second week, all sinuses and abscesses had completely disappeared, leaving behind only clean scars.

H. A. Brunsting of Mayo Clinic has emphasised the frequency and importance of hidradenitis suppurativa, (Arch of Derm and Syph 39 108-120 Jan 1939), and the following is an abridged account of that paper. Hidradenitis suppurativa is a chronic indolent, inflammatory disease of the skin and subcutaneous tissue, it is characterised by the formation of abscesses and sinuses and involves selected sites of the cutaneous surface, such as the axillary, mammary, inguinal, and perianal regions.

The disease was first described by Velpeau and Verneuil, about 100 years ago, under the title "Hidrosadenitis Suppurativa." The disease is much more common than is generally appreciated, it is obscured under such miscellaneous nomenclatures as abscess or furunculosis of the axillae, buttocks, and so forth, pyoderma, chronic, undermining, burrowing ulcers of the skin, non-specific granuloma, and fistulous disease of the buttocks.

Hidradenitis is a suppuration of the apocrine glands. The existence and distribution of these peculiar sweat glands is well known to the anatomists. The *apocrine sweat gland*, in contrast to the *eccrine gland*, is a large, compound, tubular gland which is situated at a greater depth in the corium, its distribution being restricted to the axillary, mammary, inguinal, and perianal regions. The origin is from the hair follicle, but the activity is not manifest until about the time of puberty. The apocrine glands in man are considered to be remnants of the scent glands which in lower forms are concerned with sexual attraction. The apocrine glands do not secrete sweat, instead there is exuded a cheesy, odoriferous material formed by degeneration of the contents of the glands proper. Plugging of these ducts and subsequent infection of the accumulated material

produce the abscesses and the burrowing of the skin in these selected regions so characteristic of this peculiar disease entity

Hidradenitis suppurativa is essentially a disease of adult life, the majority of patients being in the second or third decade of life. The disease, as a rule, affects robust persons who are rather well nourished and developed. It occurs without associated systemic disturbance or impairment of the general health.

Early stage The disease usually begins insidiously. Pruritus, burning, and local hyperidrosis are frequently the earliest symptoms. Later, as the inflammatory reaction increases, vague pains may develop, and a small firm subcutaneous nodule may be appreciated as the first sign of the disease. Involution of the abscess may occur without drainage, however, absorption is usually slow and the residual infiltrate may be perceptible for several weeks.

New nodules frequently appear adjacent to the original lesion. These coalesce to form a characteristic chord-like elevated band. Suppuration is usually not apparant, it is difficult to demonstrate at this stage as it is invariably deep-seated. A small pustule may be present at the summit of the nodule. Incision of the pustule usually reveals only a few drops of thick creamy pus. Drainage may continue for several days before eventual cicatrization and complete healing takes place. This is the usual course of the disease in its mild form, when only one or individual abscesses are present and when the response to treatment is favourable.

Late stage However, in the more protracted cases, suppuration may persist and extend into the deep subcutaneous tissue, with the formation of extensive sinus tracts. Frequent remissions and relapses may occur and healing may be delayed for several months. The extensive undermining and burrowing that occur throughout the subcutaneous tissues are characteristic features of the disease. Inversion and undermining of the skin margin occur with destruction of the subcutaneous fat and connective tissue, leaving epithelial bridges to connect the sinus tracts. The base of the ulcer is usually covered with healthy appearing granulation tissue, which is covered with little seropurulent discharge as suppuration extends beneath the surface. Gangrene does not occur. Fever and associated systemic reaction in connection with recurrent bouts of regional erysipelas are not uncommon. About the anus, the extension of the disease process through the deep tissue may continue with eventual perforation of the rectum and formation of anal fistula, as described by Geber as early as 1885.

Staphylococci and haemolytic streptococci are found in large numbers in infected regions, trauma, irritating lotions, eczema, plucking or shaving of axillary hair, and adenitis from infection of hands or fingers are etiological factors.

The treatment is individual in every case, and may be conservative or of a radical nature. In the early stage of the disease the two most valuable methods of treatment include prompt incision and adequate drainage, and the use of filtered roentgen rays. Local measures include a zinc peroxide paste, ultra violet rays, and sulphur

baths Sulphanilamide orally and locally is useful In far advanced cases total excision and complete destruction of all glands in the affected region and plastic repair may be necessary

Some of these patients suffer from extensive acne of the indurative type, involving the face, neck, scalp, chest, and back *Acne Conglobata* is characterised "by the presence of the constituents of acne vulgaris such as comedones, papules and pustules, and in addition large, elevated, fluctuating plaques which are dusky blue and frequently form cutaneous and subcutaneous abscesses and oil cysts, which may perforate and form discharging sinuses, healing very slowly and often leaving keloidal or so called bridge scars of Lang" Sutton and Mark consider (Jour Amer Med Assoc, April 24, 1943, p 1,344) the cases of hidradenitis suppurativa, perianal pyoderma, and acne conglobata, all to be variants of acne They do not consider these cases to be of pyogenic bacterial etiology but to be inflammatory foreign body reaction to lipid They advise a fat free diet and thyroid extract by mouth in the treatment of all these cases They record a case of acne conglobata and perianal pyoderma of ten years' duration where all sorts of treatments had failed, which responded with strikingly prompt and satisfactory results, to treatment with a fat-free diet and thyroid extract given to tolerance Improvement was observed within two weeks of starting of the fat-free regime and in seven weeks the patient was completely relieved of all symptoms in all parts of the body Low fat diet instructions The living body requires a certain number of calories If the food eaten does not contain the requirement, then the remainder is obtained by using up the body store of fat, and the one is not on a low fat diet So if one faces the alternative of either eating fatty food or going hungry one should eat Avoid all fatty foods, especially foods of animal origin, also nuts, vegetable oils, cocoa, chocolate, milk, ice cream, etc Avoid also certain rich sources of the lipid, provitamin-A-like substances tomato, chilli, cod liver oil, vitamin concentrates, spinach, carrot, sweet potato, and yolk of egg

N D P

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On the Reading Habit

Of the three well stocked rooms which it should be the ambition of every physician to have in his house the LIBRARY the LABORATORY and the ALMSHOUSE - each to benefit and train - as he may not achieve all three I would urge him to start at any rate with books and balances. Subscribe to a good weekly and good monthly journal to begin with, and read them. A Physician who does not use books and journals, who does not need a library, who does not read one or two of the best weeklies and monthlies - can sink to the level of the cross counter prescriber and not alone in practice, but in the mercenary feelings and habits which characterize a trade. The habit of reading at least one hour daily will enable you to cover an amazing amount of medical literature. I advise you to begin and to continue this habit. The more diligently and more extensively you read the more you enjoy it. For him who attains scholarship the labour of reading long since has changed to a pleasure and satisfaction. - OSLER

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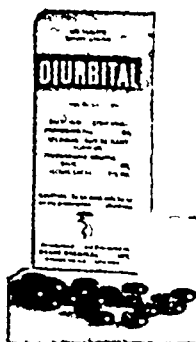
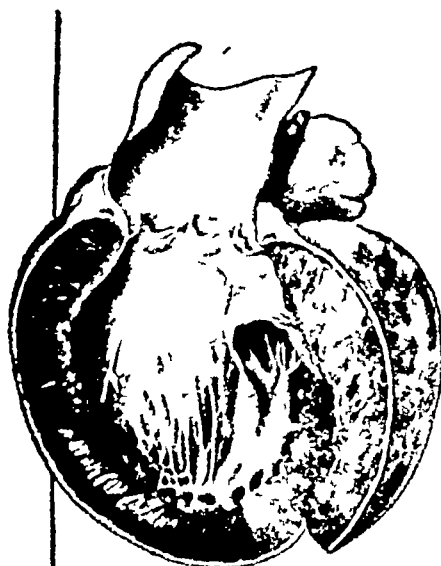


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Let us remember

EVOLUTION OF THE TREATMENT OF MENTAL DISORDERS

By

N S VAHIA

M D

BOMBAY

Mental disorders have been known to exist from prehistoric times. Mental manifestations of various disorders were regarded as being engendered by some spiritual entity or other God or Demon, which was supposed actually to inhabit the body or merely play upon it from without. If these manifestations happened to be in harmony with the religious views of the time, the controlling spirit was regarded as benign and the person was worshipped as an exceptionally holy person. If on the other hand the conduct of the individual conflicted with the ethical code of the time, he was conducted to be the victim of malignant influence. In view of such beliefs it is only natural that the treatment of such persons consisted in the use of various types of religious ceremonies. It was the custom for the mentally afflicted to visit the temple of Aesculapius where sacrifices and prayers were offered for their redemption.

Hippocrates (about 460 B C) was probably the first to try and bring about a radical change in the outlook of the laity towards mental disorders. He regarded the brain as the *situs locans* of the mud mind and to whom insanity was the result of a disturbance in this organ. He treated his patients on the line of ordinary medicine. This view, the first attempt to treat insanity scientifically, was like a cry in the wilderness and

received no enthusiastic response. It was completely abandoned within a few years of his death.

After Hippocrates, the old order was restored once again while primitive conceptions of mental disease regained popularity. Of the latter, the most remarkable in mediaeval times was the conception of "Witchcraft." Certain signs, quite familiar to the clinicians of today as those of hysteria, were regarded in those times as indisputable proofs of the unfortunate individual exhibiting the same as belonging to the much persecuted classes of witches. One such sign was Devil's Claw, a patch of insensitive skin somewhere on the body of the alleged witch, a sign frequently encountered in the present-day practice and referred to as "Hysterical Anaesthesia." Determination of the existence of the Devil's Claw sign together with certain other fantastic tests constituted the procedure of so-called "Witch Trials." This notion, which was to prevail widely over the whole of Europe for several centuries, was not abandoned in its entirety until as late as the 18th century. Many books have been written on the diagnostic features of the witches. Witches were considered to be servants of the Devil by some and as those who practise magic by others. Hundreds of suspected witches were tortured and killed in inhuman manner during this period.

With the passage of time, we witness a partial emancipation of the insane and mentally deranged. Later on as time passed these unfortunates who were no longer regarded as being the particular property of the devil, were nevertheless excluded or debarred from society. And so long as the insane was prevented from doing any harm to others the duty of the community towards the insane was discharged. This was the period during which isolation of the insane was practised, they were kept in isolated prisons or dungeons. "Men covered with filth cowered in cells of stone—cold and damp without air or light and furnished with a straw bed that was rarely removed and which soon became infectious—Frightful dens where we should scruple to lodge the vilest animals. The insane thrown into these dens were treated like convicts from prisons, loaded with chains and bound like galley slaves."

The present-day humanitarian outlook towards mental disorders we owe mainly to two factors (1) The inculcation of humanitarian ideas and (2) a parallel advance in scientific knowledge with its application to human problems. It was in

the early years of the nineteenth century that Europe reverted back to the humanitarian and rational conceptions of mental disease formulated by Hippocrates more than 2,000 years previously. Mental disorders once again came to be regarded as disturbances of brain function and attempts were made to study these disorders scientifically.

Various personalities, past and present, have left more or less permanent impressions in the history of psycho-therapy and Mesmer was one of them. Born in Vienna, in the early part of the 18th century, he practised his own methods of treating mental disorders. He was clever enough to talk of "forces," that were little understood at the time viz forces of magnetism, of electricity, of planet, nervous forces, etc. "Planetary influences," according to him, exert themselves on the human body by means of a universal fluid, a fluid in which all bodies are immersed. Sickness represents to us more than an aberration in the harmonious distribution of such fluids. Its successful treatment depends on re-establishing the lost harmony by an application of the magnetism that emanates from the living-beings. His method is called after his name, "Mesmerism."

Another personality to gain favour in America in the beginning of the 19th century was Mrs Eddy, founder of "Christian Science." Born in North America in early part of 19th century she presented from infancy, symptoms of hysterical neurosis. At the age of about 35 she slipped on ice and had a serious fall which resulted in her developing hysterical paraplegia. After an extensive trial of various forms of treatment she was finally treated by a practitioner P. P. Quimby who managed to cure her completely and almost "miraculously" of her paraplegia by simple mental treatment. It was this cure which formed the integral unit or deciding factor in the evolution of Christian Science. Quimby was a watch-maker by profession. He was interested in the subject of animal magnetism. He realised that the advice of *Clairvoyant*, where he had studied the science served only to implant in the mind of the patient the conviction of cure. Such and similar thoughts aroused great enthusiasm in Mrs Eddy. She became Quimby's secretary and plunged headlong into a study of his manuscripts, as yet incomplete on religion and spiritual medicine. After his sudden death she carried on with his unfinished work, writing freely and preaching the theories contained therein. She

inally had success in organising a sort of medical school in Boston. She charged high fees for the training which was calculated to give her pupils extraordinary ability to "make cures." This doctrine is presented in a book "Science and Health" which has by now gone into more than 200 editions. Greater part of the book is devoted to simple philosophy of life summarised in three fundamental rules: (1) "God is all in all," (2) "God is good, God is mind," (3) "God, Spirit, being all, nothing is matter." The argument often runs like this: "You say a boil is painful but that is impossible because matter without mind is not painful. The boil simply manifests through inflammation and swelling causes belief in pain and this belief is called boil. If the belief is done away with, the boil will be cured. It is the sick-mind and not the matter that holds the infection." There is no question of diagnosis because same treatment is applied in all cases.

In France, at about the same time, a new form of treatment was becoming famous—the treatment by hypnotic suggestion. In 1823 Bertand showed that movements and acts can be produced by suggestion during artificial sleep. In order to assure the success of hypnotism and to give it a practical role, a special attempt was made to use it for general anaesthesia. The discovery of ether anaesthesia which was more easy and certain, gave a fatal blow to the experiments in this direction. He used hypnotic suggestion in the treatment of neurosis and claimed great success. Between 1888 and 1896 this method of treatment was in vogue not only in France but also in various parts of Europe. After Charcot's death the science of hypnotism fell into disrepute. Physicians started discussing the dangers of such treatment—treatment that had been recommended but a few years previously as being quite inoffensive and beneficial. It was considered below the dignity of a physician to adopt the role of a miracle worker. Dubois declared that he would blush everytime he remembered his using the method of hypnosis in nocturnal enuresis of a child.

There is one line of treatment which merits a passing mention. Burq in France advised a peculiar line of treatment. His ideas have been incorporated in a book, "The Origin of Metallotherapy." He studied modifications induced by the application of metal plaques on the skin of patients and by the internal use of the same. Metal pieces suitably chosen were applied

to the skin of the insensible member and after several tremors a complete return to normal was demonstrated. At the same time, alterations in temperature, circulation, muscle force etc., were noted, finally resulting in a complete disappearance of all neuropathic symptoms. In 1876 Burq forwarded the results of his experiments to the Biological Society which appointed a special Commission to investigate their validity. The attention of the Committee was directed to the physical side of the experiment only without recognition of the psychological nature of the treatment. The experiment failed and all the work stopped abruptly.

Henrich Erb of France described the therapeutic effects of electricity. It was used for diagnosis and treatment of all sorts of diseases. Every nervous person was sooner or later initiated into the mysteries of the electric shock.

The school of psycho-therapy to which the modern psychiatrist owes most, in spite of criticism, is the Freudian school, concerning which there is much prejudice chiefly because people have come to regard Freud and Sex as synonymous. There is a big difference between rational criticism of the unproved and denial of truth just because it is unpalatable. Freud at first went to Charcot in Paris and studied hypnotism under him for two years. After his return to Vienna he talked about his knowledge to a friend of his, Breur. After hearing him Breur told Freud of a peculiar case of a woman suffering from hysteria that was treated by many doctors, but ultimately came to him as a family physician. One day she said to him "Dr Breur, if you would let me talk to you and if I could tell you how my difficulties started, I think we could do something." Breur agreed. She went on and on and curiously enough showed a tendency to recover. She had been given all sorts of medicines, hot and cold baths, electricity, and whilst talking she showed signs of recovery. This case had a great appeal for Freud. He came to a decision after much thinking that if the patient could go back to the origin of his or her symptom, the symptom would disappear. At first he tried hypnotism for diminishing the time-factor but found that some patients could not be hypnotised and in others the symptoms recurred. And so he decided to treat the patients by his own method of free association. The method consists in asking the patient "to forget that the physician is behind him, to give himself up to

all the vague thoughts that rise spontaneously in his mind and to express them as if he was alone. He should not let himself be stopped by any unexpected thought nor by any idea that seems to him futile, nor by any image or a word that is drole, fantastic or indecent. The physician should observe his subject with the most careful attention not only for ideas expressed but for the slightest detail that he can catch—hesitation, embarrassment, lapses, sighs, gestures, facial expressions etc.” To this must be added all the reveries of dreams that the patient can recover—all the memories the patient has conserved from early infancy. Thus psycho-analysis becomes a system of explanation of human psychic activity.

Brill compares hypnotism with psycho-analysis thus—“There is considerable difference between psycho-analysis and hypnotism. In hypnotism one disregards the patient’s individual make-up, and when he is in an unconscious state, one imposes upon him certain suggestions in a bold authoritative fashion. In psychoanalysis we learn to know the patient, we dwell into the deeper main-springs of his character, we gain his confidence and when we have learnt his personality and come into vital and intimate relations with him, we then remove as sculptor all extraneous matter. We impose nothing, we merely eliminate and dispense with whatever is superfluous, obstructive and cumbrous.”

Freud gathered many pupils from various parts of the world. Amongst them may be mentioned Ricklin, Ferencs, Adler, Gross, Jones, Rank, Stekel, Bleur, Jung, Medel and Brill. Freud is criticised as dogmatic, particularly regarding complete determinism as opposed to free will. Secondly in his statement that all dreams have some causative factor. Thirdly sexual desire is the fundamental desire underlying all desires and emotions. His pupils have, to a certain extent, changed his original conceptions and have established their own schools of thought. Main amongst them are those of—

(1) Jung—Unlike Freud he believes that the cause of neurosis is inadequate sublimation of spiritual ambitions. According to him sublimation is the most important single factor. If sublimation of primitive instincts is complete, neurosis would not occur. That is why, although his method of treatment is similar to the original method of Freud, he places

great emphasis on the philosophical aspects of various conflicts and aims at their sublimation

(2) Adler —An ardent pupil of Freud, he differs from him in one important respect. He believes that the background is not sex but an inferiority complex which may be due to physical, mental, social, financial, etc., factors, and the inability to overcome the inferiority complex is responsible for neurosis

(3) Meyer —He takes into consideration all factors—physiological and constitutional—that have gone into making what the individual is. He elicits the patient's history and discusses the various conflicts in relation to the psychological development and the important events in the past and recent history. The method is simpler and shorter than others

(4) Stekel —He is not guided by any definitely laid down rules. He believes in intuition and adjusts his method to the patient. His analysis is superficial, as he does not believe much in infantile materials as suggested by Freud. He even gives advice on personal matters, and how far this is advisable is open to question because thereby he imposes upon the patient his own views and it is a claim of psycho-analysis that it insists on the freedom for the patient to make his own decisions

Last 10-20 years have seen considerable advance in another direction. All this treatment mentioned above can be undertaken for those that respond to environment, but for those that had lost contact with the surroundings the treatment was an acute problem. As late as the beginning of this century the psychiatrists were discussing the value of psycho-analysis in the treatment of these conditions and although most of them considered this as useless (or even harmful) some workers like Jones and Jung and Diathelm maintained that in selected early cases, psycho-analysis had some place in the treatment of Dementia Precox. Wagner-Juragg was perhaps the first who brought about some change in the outlook. In 1897 he conceived the idea that suppuration or fevers improved the mental conditions of patients suffering from general paralysis of insane. He waited for twenty years before he put his theory into practice and in 1917 he inoculated malarial parasites into nine paretics out of whom six improved with good results. Encouraged by the results, he treated bigger series in 1919 and 1922 and published good results. Although some change has occurred in the technique of producing pyrexia, pyrexial therapy is now an esta-

blished line of treatment for this condition. Others observed that coma due to any cause also brought about some improvement in mental condition of the insane and so a method was evolved of producing coma artificially by causing hypoglycemia by insulin injection. The coma lasts for about an hour and then by administration of glucose the patient comes to normal. This treatment is found to be useful in more than 60% of cases. It was noted for a long time that the co-existence of Schizophrenia and epilepsy was a rarity and it was noted by some psychiatrists that when convulsions occurred due to any cause, the mental condition of schizophrenic showed improvement and thus attempts were made to produce convulsions artificially in these cases. The attempts were successful. At first cardiazol was tried. And it is still the drug of choice. A series of convulsions are produced under medical supervision at regulated intervals. In a large series treated with metrazol improvement was noted in more than 60% of cases. It has more lately been found that electrically produced convulsions are more easy to manage and are simpler to induce. Electrodes are applied to the forehead and a current of about 100 volts is passed for 0.1 to 0.2 second. As far as it is known there is little chance of permanent damage to the brain. The convulsion therapy on the whole is not without danger. It is contra-indicated in cases of cardio-vascular syphilis, atherosclerosis, chronic nephritis, tuberculosis etc., and is known to produce dislocation of jaw, fracture of limbs, status epilepticus, cerebral haemorrhage, etc. In acute melancholia or mania, prolonged deep sleep is found to be beneficial. Sleep is produced by various injections e.g., sodium amytal, evipan, paraldehyde, and with interruption of about 8 to 12 hours interval, is made to last for about 7 to 14 days.

It has been found that certain mental disorders occur because of endocrine dysfunction and hormone-therapy is found to be useful in these conditions. The use of thyroid in cretins and myxoedema cases, extracts of suprarenal cortex in lethargy of Addison's disease, ovarian follicular hormone in involutional melancholia, testicular extracts in so-called male climacteria is recognised.

Vitamins also are of importance in certain conditions e.g., Nicotinic acid in dementia of pellagra, vitamin B₁ in Wernicke's syndrome.

Electro-encephalography is still in its infantile stage but in the next few years it may play a great part in the diagnosis and treatment of mental disorders. For example, definite rhythms are described in patients suffering from epilepsy, different types being found in petit-mal and grand-mal. Such rhythms are not found in hysterical convulsions. At present, it is believed that there are no specific changes in psycho-neurosis, but it is perhaps too early to be dogmatic about a method of investigation that is still under development.

Lastly we look upon the present war with great hope that out of all its chaos the psychiatrists will find vast material for research. Under the stress and strain of war, mental disorders of various types flourish not only in men on the battlefield but also amongst civilians. Large numbers of articles by various workers are appearing from day to day and let us hope that by the end of war the sum and substance of all such work may lead to considerable advances in the treatment of mental disorders.

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Original Contributions

TREATMENT OF ACUTE OPIUM POISONING AND

CORAMINE (Nikethamide)

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The literature from the West dealing with cases of acute opium poisoning is very meagre, because the incidence of such cases is very low, particularly when compared to countries like China and India. Difficulty in obtaining opium, and the other means in vogue for committing suicide, and the ease with which they are available, drift the people away from opium. Publication of the results of various forms of treatment instituted, in acute cases of opium poisoning by workers in the Orient would therefore be the main source of information for the medical profession. I have therefore gathered the following report from the cases of acute opium poisoning admitted to K. E. M. Hospital, Bombay, during the years 1939 to 1942. Fifty such cases have been admitted during these four years.

The incidence of cases of acute opium poisoning had fallen during 1940 and 1941, as the people could not easily procure the drug during these years due to the prohibition policy of the Government. 1942 showed a rise, although it did not reach the former level of 1939. The mortality rate shows varying figures during the different years. Our case mortality of 50% in acute opium poisoning compares very unfavourably with that of 29% in Medical Union Hospital, Peiping. Perhaps less of opium addiction in Bombay as compared to Peiping, indirectly leads to suggest that the greater percentage of suicide cases by ingestion of opium occur in Bombay, than that occurring in Peiping. This suggests that a case of acute opium poisoning is of a more severe character, when opium has been taken for the first time than the case in which there is merely a transgression of the habitual daily dose.

TABLE I

Year	No of cases admitted	No of cases expired	Mortality percentage
1939	23	6	26.1%
1940	5	4	80%
1941	—	5	71.4%
1942	15	10	66.6%
Total 1939-42	50	25	50%

The effect of whatever form of treatment that may be instituted will depend upon many factors. Onset of coma and its duration before the treatment is begun, are the two main factors, besides others, of prime importance, to be taken into consideration. Pulmonary oedema, the state of pupils, and the degree of the depression of the respiration are the other factors of prognostic significance, which should be considered.

The absorption of opium depends upon varying factors such as the form in which the drug is ingested or instituted, the nature of the gastric contents and the presence or absence of pyloric spasm. A lump or a pill naturally takes more time to be absorbed than a solution in the form of tincture, or in any other form. The absorption is better on an empty stomach and the presence of food material hinders absorption. Presence of pyloric spasm which may exist even if the patient is comatose, keeps the poison in the stomach for a long time. This fact, coupled with the fact that the absorbed opium is supposed to be excreted in the stomach, makes gastric lavage a very important step in the prevention of further absorption of opium. When the drug is absorbed in sufficiently large doses so as to hold in abeyance all except the vital functions of the body coma ensues. It is one of the criteria which indicates the severity of the form of poisoning. The duration of coma is another criterion to go by. Longer a patient is comatose, before the treatment is instituted, the greater is the danger of irreparable damage to the cardiovascular system. This damage together with the prolonged and intense depression of respiratory centre which exists in cases of opium poisoning may precipitate a much dreaded complication viz., pulmonary oedema.

In the present series twenty-three cases (46%) out of a total of 50, were admitted in an unconscious condition. The remaining twenty-seven (54%) were either semi-conscious or drowsy. Out of 23 comatose cases that were admitted, 17 died. Whilst from among the 27 non-comatose patients only 6 died. There-

fore, the mortality rate of comatose patients was 73.9% whereas that of non-comatose patients was 22.2%.

TABLE II

	Comatose patients	Non comatose patients
Numbers of patients	21	27
Numbers expired	17	6
Percentage mortality	73.9%	22.2%

Mortality rate of comatose cases found in Peiping by Snapper and others is very much akin to that found in the present series. Their average for the period of ten years between 1930-40 was found to be 71% as against 73.9% in our series. This similarity of figures assumes a very great importance, particularly when we learn, that a sharp fall has occurred in their mortality rate after they began to treat their cases with Coramine (Nikethamide). Mortality of 46 comatose cases treated with coramine was only 26.1%. This was significantly different from 74.4% before coramine treatment was started. Coramine therefore suggests itself as a mode of treatment for the cases of acute opium poisoning, because it was mainly responsible in bringing about this remarkable fall in the mortality of comatose cases.

One of the characteristics of a case of opium poisoning is the state of its pupils which are remarkably contracted and do not react to light. These pin-point pupils, however, give way to dilatation in the last stages of poisoning. Whatever be the form of treatment instituted, it is found that when the pupils are dilated, death is certain. Only three cases out of 50 in this series showed dilated pupils. Of these, one was complicated by intracranial haemorrhage. Of the remaining two, one succumbed within 20 minutes and the other, 75 minutes of admission. Out of the 12 patients that Snapper lost during his coramine period, 4 showed dilated pupils. Life saving effect of coramine is therefore limited to patients of opium poisoning so long as their pupils are not dilated.

Another grave sign that almost always heralds death in case of opium poisoning, is pulmonary oedema. In our series of 50 cases, 7 developed signs of pulmonary oedema, and all these expired. Five of these survived less than two hours after admission. It is found that a patient may survive, even if there is complete cessation of respiration for a short period, if properly treated, so long as pulmonary oedema does not set in.

What is undesirable is not so much of depression of respiration, as the onset of pulmonary oedema. Considerable increase of the venous pressure, which has been observed in experimental animals with morphine poisoning, is a constant feature of the cases of opium intoxication. Gastric lavage which is usually accompanied by gagging and struggling must be highly deleterious to the damaged heart of the patients and may well precipitate the onset of pulmonary oedema.

Opium has a depressant effect on the respiratory centre, the severity of a case of opium poisoning will therefore be shown by the degree of depression of respiration. The greater the depression, more severe is the form of poisoning. The degree of depression of respiration, therefore, is another criterion to go by, when gauging the effect of coramine in cases of opium poisoning. Out of 34 survivors during the period of coramine treatment, Snapper found that 10 cases showed Cheyne Stokes respiration and in 4 patients the breathing had even completely stopped. These figures stand prominent when we find that out of our 25 survivors not one showed Cheyne—Stokes breathing and only 2 cases showed a respiratory rate below 10 per minute. Snapper's figures of cases before he started the treatment could be compared with ours. The striking contrast in our figures now existing can only be attributed to the beneficial effect of treatment with coramine.

Whatever be the details of the treatment, the following is the basis on which the treatment of a case of acute opium poisoning is carried out. The aims of treatment are (1) Removal of as much of opium that may be present or be excreted into the stomach, (2) Restoration of the depressed respiratory function, (3) Maintaining the strength of cardio-vascular system, and (4) Prevention of respiratory complications such as bronchopneumonia, pulmonary oedema, and lung abscess.

Removal of opium that is remaining or is being excreted into the stomach is fulfilled by the stomach wash. Gastric lavage, given immediately after a case is diagnosed as that of opium poisoning, forms a routine in K E M Hospital. All the cases in our series were given the wash, half hourly with potassium permanganate solution diluted with five times its quantity of warm water, leaving 5 ozs of the diluted solution in stomach. The lavage should not be undertaken lightly and without proper lowering of the head as the danger of subsequent development

of bronchopneumonia is very great. To minimise the danger, nasal catheters may be used instead of the stomach tube and 5 oz, of the oxidising solution may be administered every few minutes. The nasal catheterisation is also believed to minimise the possibility of pulmonary oedema setting in, by avoiding the struggle accompanying the gastric lavage, and consequently saving the damaged heart from an extra burden which is very likely to precipitate the pulmonary oedema. Potassium permanganate solution oxidises the portion of the drug which is still remaining in the stomach due to pyloric spasm, and has not passed into the duodenum. The part of the solution that is left behind, deals with the drug that is excreted into the stomach subsequently and prevents its further effect by rendering it innocuous.

It is sometimes found that patients, who are still conscious when admitted, become deeply comatose during the lavage. This can be explained in the following way. At the time when these patients are still conscious, the function of respiratory centre is already depressed. The hyperpnea which follows the introduction of the stomach tube, and the gastric lavage with several pints of the potassium permanganate solution causes a certain amount of apnoea, sufficient to induce cessation of respiration in these patients with a damaged respiratory centre.

To bring about the restoration of the respiratory function, a number of drugs were used in our series of cases. Of these Caffeine et Soda benzoas, coramine, strychnine, camphor in oil, lobeline, and cardiazol were quite frequent. These drugs were however used as general respiratory stimulants. The very fact that so many drugs were utilised to bring about the restoration of the respiratory function, suggests that the drugs used were not so much as the specific antidote in opium poisoning, as they were general respiratory stimulants.

Of these drugs Caffeine et Soda benzoas seemed to be a greater favourite in our series. Twenty-four cases out of 50 were given the drug. Nine of these 24 were admitted in a comatose condition, out of which 2 survived. Analysing those who did not receive the drug we found that out of 26 patients, 14 were comatose and out of these 14 comatose patients only 2 survived. The survival rate in the comatose patients treated by Caffeine et Soda benzoas was 22.2% while in those not treated by this drug was 14.3%.

TABLE III

	Cases treated by Caffeine et Sodii Benzoas	Cases not treated by Caffeine et Sodii Benzoas
Numbers of cases treated	24	26
' coma cases	9	14
' cases that expired	9	16
' comatose patients that survived	2	2
Survival rate in coma cases	22 2%	14 3%

This greater survival rate, however, seems due to the fact that out of all the drugs used in the series, Caffeine et Sodii benzoas was the only drug used with sufficient dosage and frequency, to bring about whatever little good that may accrue from the proper exhibition of a general stimulant. Its good effect may partly be accounted for by the action of Caffeine on the damaged heart. These figures, however, do not take into consideration all the factors that are important to give us an approximate estimate of the effect of Caffeine et Sodii benzoas. Out of the two survivors who were given Caffeine et Sodii benzoas, one had received 6 c c of coramine and the other had 10 c c of cardiazol intravenously. The cause of their survival may well be, to a certain extent at least, due to the effect of these drugs than Caffeine itself. Therefore Caffeine et Sodii benzoas does not rightly deserve a very important place in the treatment of acute poisoning though it can well be utilised as an additional stimulant, more due to its effect on the heart than on the respiratory system. The dosage and frequency with which the drug was given varied considerably from case to case. They varied from 1 c c to 4 c c and were repeated very often 4-6 hourly during the first 24 hours. From the next day onwards, only one dose varying from 1 c c to 2 c c was given daily for one or two days. Camphor-in-oil was used in seven cases. Lobeline was used only in 3 cases. These were seldom repeated and their use was so restricted that it could give us no definite idea about their beneficial effect in cases of opium poisoning. Similar was the case of strychnine which was given in 10 cases.

Cardiazol was administered to 6 patients of which 4 were comatose. Three of these four patients died. In 5 out of the 6 patients it was given together with Caffeine et Sodii benzoas. It was, however, found to be the only drug which was attempted more as an antidote in opium poisoning cases, than any other drug used in our series. Its analeptic effect was utilised actually to the extent of procuring convulsions for two minutes. In one

case 2 cc of the drug was given intramuscularly and 20 cc later on intravenously within an interval of 2 hours and 30 minutes. The pupils were contracted and his respiratory rate was 20 per minute. Yet, the convulsions thereby did not help the patient and he died about 4 hours after admission. In another patient 24 cc of the drug injected intravenously during a period of 9 hours did not save the patient, who was comatose with pinpoint pupils and respiratory rate 5 per minute. Even though, these cases belong to the group of cases with severe form of poisoning, yet we can say that the results achieved by cardiazol were not very encouraging in cases of acute opium poisoning. Further evidence should be forthcoming before we completely discard the drug with its analeptic effect, from the treatment of opium poisoning.

Another drug which was very often used was Coramine. Its dosage and frequency, however, were restricted, as if it were being used more as a general stimulant than as an antidote in opium poisoning. Twenty-three patients were given coramine. Fifteen of these were comatose out of which 12 expired. Twenty-seven cases received no coramine. Eight of these were comatose out of which 6 expired.

TABLE IV

	Numbers treated by coramine	Expired	Numbers treated without coramine	Expired
Comatose	15	12	8	1
Non comatose	8	1	19	6

These figures take no account of the degree of the depression of the respirations and the state of the pupils, the two important criteria to judge the severity of poisoning. They, however, supply us an information, that coramine when used in a single small dose as was usually done in our cases, proves of very little benefit in cases of opium poisoning. Only four cases were given more than 5 cc of coramine and in no case the total amount given exceeded 10 cc. By far the greater majority received only 1-7 cc. The uselessness of a single small dose will be more evident when we contrast our results with those of Snapper and others who used the drug repeatedly and in large doses.

Maintenance of the strength of the heart, which is damaged by sudden increase in venous pressure, and enhanced by damaged and congested lungs with deficient movement, is accomplished

by intravenous administration of a drug belonging to digitalis group. This should be given during the first 24 hours after the admission, particularly when the pulse is rapid and feeble.

Another danger that should be guarded against in cases of opium poisoning, is the development of aspiration bronchopneumonia, during the convalescent period. In fact it is stated that incidence of aspiration pneumonia is highest in the cases of opium poisoning than in any other case. Prolonged depression of respiration, together with constant lying down in bed for days together, devitalises the lungs which fall an easy prey to infection, and give rise to bronchopneumonia. As an additional factor, which augments this devitalisation and helps the subsequent infection, gastric lavage stands out prominently. The administration of sodium sulfapyridine as a routine, is undertaken as a combating measure to avoid bronchopneumonia during the convalescent period.

Snapper advocates the use of sulfapyridine in conjunction with coramine and believes that coramine is more effective together with sulfapyridine than when it is used all alone. He has, however, no statistical data to quote in favour of or against this statement. It is quite probable that several of those who survived might have developed bronchopneumonia if no sulfapyridine was used. We have no precise information of any development of bronchopneumonia, in our cases in which no sulfapyridine was used and which were discharged within 4 days of their admission, if they came round from the effect of opium poisoning.

Pulmonary oedema, as already mentioned, is another treacherous complication, and an attempt at its prevention is made by a routine administration of atropine. Almost all our cases were given atropine, which has an analeptic effect so far as respiratory system is concerned.

From the above paragraphs, it can be seen that the main obstacle offered, in the treatment of acute opium poisoning is the respiratory depression. It is therefore not out of place to consider the various analeptics used to restore the respiration. Analeptic, a term fast disappearing from the scientific medical literature may be defined as a pharmacological agent acting primarily and sometimes electively upon certain region and section of the nervous system and certain peripheral organs, so that their functions are stimulated. Certain purine derivatives

(caffeine and theobromine), strychnine and camphor belong to this group. Adrenaline and pituitary extracts under certain conditions and atropine, so far as the respiratory system is concerned, can be enumerated under this heading. Of these, purines have sufficiently known demerits to enter into a discussion. Camphor quickly forms oxidation products in the body which unite with glycuronic acid and sulphate and form inert compounds. Such obstacles encouraged a study of organic compounds, whose chemical constitution promised to materialise our needs. Certain carboxylated pyridine derivatives showed many actions closely allied to those produced by camphor itself. Among the bodies of this group it was found that, nikethamide or pyridine- β -carbonic acid diethylamine (the trade name of which is Coramine), has in man and warm blooded animals, the desired camphor-like action in the most pronounced degree. Faust found that it produces an increase in the respiratory rate with rise of blood pressure due to stimulation of medullary centres. Toxic doses produced tremors, excitement, and finally convulsions. There is also an increase in the respiratory volume. As compared with strychnine, it has a great advantage that its main action is exerted principally in the autonomic centres in the medulla, while strychnine acts mainly on the spinal centres. Another great advantage is the fact that nikethamide has no cumulative action. It is also found that its effective therapeutic dose is far below its toxic dose. Faust holds that nikethamide bids fair to prove a valuable substitute not only for strychnine but also for camphor and caffeine, in as much as its stimulating action is exerted equally and simultaneously on central nervous system and on the circulatory and respiratory apparatus.

For these reasons, coramine has been widely used as a stimulant for the respiration and circulation and has been specially recommended for cases of overdosage with avertine, morphine, and in barbiturate poisoning. As a result of the clinical data Kennedy confirms Kilian's view that coramine is an effective agent in counteracting the cardio-vascular depression due to overdosage in avertin anaesthesia. It was found, however, that picrotoxin fared better, in these cases, as a respiratory stimulant. Though picrotoxin has an excellent effect in barbiturate and avertin intoxication, in experimental opium poisoning it was found that coramine and metrozol are more

potent stimulants of the respiration. Already in the first publication about coramine, Ulhamann in 1924 emphasised that the depression of the respiration caused by morphine poisoning in the rabbit, can easily be neutralised by coramine. After the administration of coramine the deeply narcotised animal wakes up and seems completely normal. The action of coramine, however, is of shorter duration than that of morphine and therefore it is usually necessary to repeat the injection of coramine. In view of these experimental results Ulhamann advised trying coramine in morphine poisoning. The experiments of Maloney and Tatum confirm the results of Ulhamann.

Armed with this knowledge, Snapper, Chu and Ching started administering coramine in case of acute opium poisoning. Intravenous injection of 5 c.c. of coramine, usually to be repeated several times, was found to succeed in reviving the respiratory centre and restore the consciousness. This also brought down the mortality rate of comatose cases in acute opium poisoning which previous to the administration of coramine fluctuated between 70% and 80% to about 26% after the treatment with coramine was started. This fact should be an eye-opener for us, in India, where our present mortality rate still compares very unfavourably with the mortality rate of Snapper's cases after he started the treatment with coramine.

In conclusion, it is suggested that in nikethamide we have found a valuable addition to our armamentarium against opium and other depressant poisons and its adequate and proper use would go a long way in helping us to reduce the mortality of these cases which is still fairly high in our country.

I would like to express my thanks to Dr R. P. Koppikar, Dean K. E. M. Hospital for allowing me to publish this report, and to my Chief Dr N. D. Patel, for suggesting this investigation and general guidance.

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OBSERVATIONS ON "TROPICAL" EOSINOPHILIA

By

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CLINICAL PATHOLOGIST

B O M B I I

Before I offer my observations on "Tropical Eosinophilia," I should like to say that the credit of being the first to have his collected cases of eosinophilia published in the *Lancet* (6230, Jan. 23, 1943, 103), goes to *Weingarten*

While *Weingarten* has chosen the name "Tropical Eosinophilia," *Major Owen* has suggested the name "Eosinophilic Lung" apparently for the same condition. Whether the condition met with in this part of the country is peculiar to and confined only to certain latitudes of the tropics, and whether it has clearly recognisable 'important factors which mark Tropical Eosinophilia as a new disease entity,' or not, must remain to be finally decided in the future, in the light of further more detailed and well considered data. The name "Tropical Eosinophilia" is only a descriptive geographical nomenclature while the name "Eosinophilic Lung" is better in so far as it lays stress on the chief underlying pathological condition and its primary focal infiltrations in the lung. At the moment, one feels that both these names are as good or as final as the names "Epidemic Influenza, Heine-Medin Disease, Poliomyelitis superior, and Botulism," applied to the Influenza-like deadly epidemic that had broken out in England during the World War No I, in 1918. The confusion about nomenclature created at the time was so great that at last the *Lancet* had to suggest the name "Obscure Epidemic Encephalitis," under which heading my observations at the London Hospital were published in the *Lancet* of September 7, 1918. It was only after one more year's searching aetiological inquiry and experimental research that the disease was finally named "Encephalitis Lethargica." Such being the experience, one would be reluctant to jump to hasty conclusions. In this connection it may seem necessary to utter a word of caution in the danger of undue stress on the high

degree of eosinophilia and on the findings and interpretations of x-ray pictures. We must not lose sight of the fact that x-ray investigations are of recent date and the findings, whatever they be, can only add to hitherto recorded facts regarding this condition and cannot possibly detract from their value in determining its nature. It does not require now to stress the point that any asthma-like condition coming on with bouts of cough without any sputum, accompanied by dyspnoea and wheezing sounds at night if on investigation it showed marked eosinophilia in blood and also in sputum, it would be diagnosed as bronchial asthma. It does not follow that because the eosinophilic response is extremely pronounced, the condition cannot be asthma and should on that ground be considered to be a separate disease entity. Both the x-ray findings and the pronounced eosinophilic blood-picture in my judgment are only an index of the degree of response and not of the quality of that response. It is now generally accepted that asthma and allied conditions are allergic manifestations caused by different allergens and the degree of response naturally depends upon the nature of the allergy-causing agent both as regards its virulence and peculiar individual characteristics. All cases of pneumococcal infections do not behave alike in the quantitative (or degree of) response of polymorph-neutrophil-leucocytosis, and for that reason alone they cannot be classed as separate disease entities. The same applies to the eosinophilia excited by the allergens and the quality of the response and not the degree would be a valuable supporting point in diagnosis. Even in old books one finds mention of "eosinophile" bronchitis, (Sahl, second Eng Ed, 1920, p 808), while Simon (Clinical Diagnosis, 9th Ed, p 590) mentions eosinophilia of 53.6% and total leucocyte count of 52,000 per cmm in bronchial asthma. Sajou (Cyclopedia of Medicine, seventh Ed, 1915, p 224) also records a case of asthma with 41,000 total leucocytes and 72.5% eosinophils. As is already published in the *Indian Physician*, (Vol II No 9, Sept 1943, Heilig and Visveswar, pp 305, 309, Owen p 312 and Patel, p 333) Price, Löffler and Naegeli have mentioned "eosinophilic leukaemia," "eosinophilic lung infiltration," "eosinophil catarrh" and "pulmonary infiltrates with eosinophilia," in cases met with in Europe, and Karan and Singer have reported similar conditions in America. It would thus appear that the eosinophilic conditions are by

no means confined and peculiar to the tropics. The obvious conclusion is that the conditions are the same in their allergic causation, that they are all due either to the same or an allied allergen, and that the allergen as judged by the clinical histories recorded is more likely to be an air-borne virus of vegetable origin. Until such time when it can be definitely settled whether this condition is a separate entity or not, it would be wiser to keep an open mind. That organic arsenical preparations like neosalvarsan have been found to relieve or even practically cure this condition, cannot by that reason alter the underlying nature of the disease. All that it would imply would be that a new treatment has been found for bronchial asthma or an allied condition, just as in the case of syphilis.

Weingarten states that during his five years' practice in Bombay, he was not aware that this disease was at all known or at all under investigation, although he understood later that "asthma" was occasionally treated with soamin without, however, discriminating between different types of "asthma".

I believe him when he says that he was not aware. Of course it is a pity, but I am not surprised. The explanation probably is that his not having a 'registrable qualification' might have come in the way of his coming into contact professionally with members of the local medical profession owing to reasons of medical ethics, and thus he might have remained unaware. But the facts are that in Bombay, cases of asthma-like conditions were being investigated, radiologically, haematologically, clinically and finally by therapeutic test. Practically every wide-awake practitioner, whether general or consultant, knows and knew that asthma-like conditions were found many times clinically to suggest asthma, and radiologically to suggest tubercular infiltration, but on sputum and blood examination, they were found to be associated with very marked eosinophilia both in blood and in sputum. And therefore these were finally grouped as Allergic Conditions like asthma.

I may say that being a clinical pathologist I am myself not undertaking treatment of any cases personally, but even so I had learnt from my friend, G. V. Deshmukh, M.D. (Lond.), F.R.C.S. (Eng.), *in the middle twenties that cases of asthma with marked eosinophilia responded very well to injections of 0.3 gm. to 0.45 gm. of neosalvarsan given intravenously,*

and even one or two injections often did much good. In my laboratory case-records of the last 20 years, there are well over a hundred cases of very marked eosinophilia with history of asthma-like attacks. Naturally there are no cases treated by me but I have always suggested to my medical friends the use of intravenous neosalvarsan on general principles in cases of marked eosinophilia with cough. I give below, by way of illustration, some such cases among friends and relatives that were investigated by me haematologically and were treated by others with neosalvarsan.

ILLUSTRATIVE CASES

1929

Case 1—N K B, Male, Age 48 years, Hindu Brahmin, strict vegetarian, Educationist, came from Bhavnagar in Kathiawar, for investigation. He was getting low fever with hacking cough, with asthma-like attacks at night. As he was losing much weight, it was suspected that he might after all be suffering from T B Lung, and was advised to get himself thoroughly investigated in Bombay in July 1929. Being a personal friend, he naturally came first to me, and as I was preparing to take his blood for a count, I was struck by the difficulty in breathing even in the afternoon while sitting, and by the harassing dry cough that he was trying so suppress and could not. The blood count was as under—

1st July, 1929	RBCs	4,000,000 per c mm	Hb
75% (Corrected Sahli), C-I		0.94 WBCS	45,333
per c mm	Very marked increase		

Differential leucocyte count (200 cells)

Poly-neutrophils	Lymphocytes	Hyalines	Eosinophils	Mastcells
12.0%	6.0%	3.5%	77.0%	0.5%

Such being the findings I was really happy and assured my friend, that he was positively not suffering from T B Lung and would be all right if he took one or two injections of Neosalvarsan intravenously. He was given one injection of 0.3 gram neosalvarsan next day by Dr G V Deshmukh and within a few days he felt so well that he decided not to take any more injections and went back to his place. I have been in touch with him throughout the period and can say that he has not had any recurrence and is quite well today.

1931

Case 2—D D, Male, age 42 years, from Bhavnagar, Kathiawar Hindu, Nagar, strict vegetarian. Gave history of "Asthma". Total white cell count was not done but the differential leucocyte count on 4-4-1931 was as under (200 cells)

Pol. neutrophils	Lymphos	Hyalines	Eosinophils	Mastcells
12.5%	16.5%	2.0%	69.0%	0.0%

He was also advised to take Neosalvarsan injections and after treatment was well

1931

Case 3—M D S, Female, age 20 years, non-vegetarian of Bandra, Bombay Temp 99/99 6°F Irregular, three months ago—'Congestion of lung' with phlegm and temp 101 6°F Otherwise no complaint Married 3½ years ago, not been pregnant Pulse rate in Laboratory—89 p.m with temp 99°F Front of neck rather full

The blood-picture was as under on 6-7-1931

RBCs	Hb	C-I	WBCs	Polymer	Lympho	Hyalin	Eos	MC
475/ Ml (c m m)	95%	10	14,000 per c mm	19.5%	32.0%	3.0%	45.5%	0.0%

My note on the report to the attending physician says —Marked eosinophilia Usually met with in Asthma cases in Bombay

1934

Case 4—V R V, Female, age 20 years, Hindu, strictly vegetarian Comes from Kathiawar, Rajkot and Jamnagar and is descended on her mother's side from an asthmatic family Has hacking cough, with low temperature and asthma-like attacks with distress at night lately

The Blood picture on 23 5-34 was as under

RBCs	Hb	CI	WBCs	Polys	Lump	Hyal	Eos	MC
1.5 Mill	80%	0.9		16.0%	24.5%	1.0%	57.0%	1.5%

She was advised intravenous neosalvarsan and two injections of 0.3 gms at weekly intervals were given to her by Dr Ramnik Vaidya, which set her right The following are her further counts, showing a relapse in 1938

Date.	Total WBCs	Poly	Lymph	Hyal	Eos	MC	Remarks
31-5-38	35,000	14%	16%	3%	65%	0%	Has asthma-like cough
26-2-41	10,200	50%	28%	3%	19%	0%	do, also gets temp 101°
20.9.41	6,200	39%	13%	8%	10%	0%	Feverishness, still has bouts of cough and discomfort now and then

1934

Case 5—M H M, Male, age 10 years Muslim, non-vegetarian

The Blood-picture on 31 July, 1934 was (400 cell count)

RBCs	Hb	C-I	WBCs	Polys	Lymph	Hyal	Eos	MC
4.3 Ml	80%	0.93	22100	10%	22.25%	4.00%	63.25%	0.50%

The note to the attending physician drew attention to the marked eosinophilia, both relative and absolute And arsenical injections were suggested

I may state here that in the very nature of laboratory investigations in private consulting practice it is but rarely that one gets a chance of either repeat examinations to check and note the treatment response in blood picture But luckily one gets an occasional case in which the question of payment of fees is not involved, when the case could be followed up by repeat examinations I give one such illustrative case below

1934

Case 6—Mr X male, age 35 years, Hindu, not strictly vegetarian. A leading surgeon in Bombay. A colleague and friend. Was suddenly taken ill some time after a trip to Kathiawar and Rajputana, with temperature 100.4°F, diarrhoea, lightening headache and pain in all the muscles of the body, more marked in muscles of the chest, slight wheezing respiratory sounds, and very prostrate

Investigations begun on 1-10 1934

Date	Total WBCs	Differential Count					Remarks
		Poly	Lymph	Hyal	Eos	MC	
1-10 34	14,400	54%	16%	5%	25%	0%	Temp 100.4°F Hastaken Quinine
2-10 34	17,950	40%	15.5%	3.5%	41.0%	0%	Rising Eosinophilia
8-10 34	45,300	15.0%	10.0%	1.0%	72.0%	0.5%	Temp 100°F
12-10 34							Suggested neosalvarsan in view of rising eosinophilia 12-10 34 But only sulpharsenol 12 cgm given

Trichinosis was considered at a consultation between six colleagues and possibility was kept in mind, although there was no history of infection through food.

It was desired that laked blood samples be searched for larvae of trichinella, but none were found. Sputum examination revealed 10% eosinophils.

In view of the negative Trichinella Larvae finding, the attending physicians decided to give Sulpharsenol 12 cgm intramuscularly and not neosalvarsan.

Date	Total WBCs	Differential Leucocyte count					Remarks
		Poly	Lymph	Hyal	Eos	MC	
13-10 34 (after sulpharsenol)	60,450	12.00%	10.66%	1.66%	75.66%	0%	Temp 101°F
18-10 34	56,600	4.75%	6.75%	1.50%	87.00%	0%	Temp 101°F
22-10 34	49,338	7.25%	5.00%	3.50%	84.25%	0%	Deshmukh and I again press for neosalvarsan intravenously O 15Gm neosalvarsan injected 24 hours ago
24-10 34							Wassermann Reaction found negative
25-10 34	87,833	5.20%	7.00%	0.80%	87.00%	0%	Temp slowly coming down, feeling better more cheerful. Not dependent as before. They propose giving O 3 gm neosalvarsan today.
29-10 34	25,766	13.0%	9.7%	2.3%	75.00%	0%	O 3 gm injected 3 days ago temp 98/99 looks better. Says feels better and now likes to read.

Unfortunately my friend the late Dr Y. G. Nadgir was very ill at Dharwar and I had to leave Bombay on 30-10-1934, and thence

to Kathlawar On my final return on 16-11-1943 I learnt that the patient had left for a Hill Station Thus I was not able to follow the case further to final disappearance of eosinophilia

Since his return from the Hill Station he had been working regularly without any discomfort for over three and a half years and there was no occasion for further blood examination But during March 1938 he had a *relapse* with very similar symptoms On examination his blood showed eosinophilia and after five injections of neosalvarsan intravenously, he felt quite well again, and as a matter of fact he felt so well only after the second injection, that he joined duty in spite of his total leucocytes standing at 22,300 and relative eosinophil count being 72% He had *another relapse* with similar symptoms again strangely enough after another period of three and a half years during October 1941 And he became again well after a course of six neosalvarsan injections during three months His last count was done on 18-9-1943 only a fortnight ago as he had a premonitory feeling of a relapse coming on and he took an abortive neosalvarsan injection after the count, as there was a total leucocyte count of 16,000, although there was no eosinophilia

The details of blood-counts and treatment during the relapses are given below —

First relapse							Remarks
Date	Total WBCs	Polys	Lymph	Hyal	Eos	MC	
21-3-38	12,400	51 5%	17 0%	7 0%	24 5%	0%	Wheezing sounds feverish Pain in transverse colon
After NeoSalv							
28-3 38	28,400	18 0%	13 5%	3 0%	65 5%	0%	After O 3 gms neo salvarsan
4-4-38	22,300	11 5%	15 5%	1 0%	72 0%	0%	After second inj neo salvarsan O 45 gm felt better and joined duty
11-4-38	17,950	12 5%	15 5%	1 0%	71 0%	0%	After third O 45 gm inj neo salv ar
20-4 38	10,050	10 5%	27 0%	3 5%	29 0%	0%	After fourth inj O 45 gm
10-5-38	9,250	66 0%	19 0%	5 0%	10 0%	0%	After fifth O 45 gm neo injection

He was now quite well and remained so until September 1938 when he got an attack of fever with seediness like that met with in ordinary influenza, but as he was afraid lest it might prove to be another relapse, he came up for a count which was as under

Date	Total WBCs	Polys	Lymph	Hyal	Eos	MC	Remarks
5-9-38	8,350	62%	24%	6%	8%	0%	He did not feel worse and no neosalt taken

Blood-picture and treatment during second relapse during October 1941

Date	Total WBCs	Poly.	Lymph	Hyal	Eos	MC	Remarks
28-10 41	10,200	62 5%	24 5%	8 5%	4 5%	0%	Temp cum shivering No malarial parasites found, was taking quin orally He felt worse a few days later and took O 3 gm neosalt. inj

After commencement of treatment

							Remark
14-11-41	37,500	55%	8%	10%	85.5%	0%	Cough, wheezing sounds, abdominal & chest discomfort
19-11-41	31,600	90%	12.5%	15%	77.0%	0%	After second inj neo 0.80 gms Feels & looks better
30-1-42	6,400	55.0%	35.5%	5.5%	4.0%	0%	After a course of four neo injects
He felt well again, but on 22-7-1942 he again felt seedy with temperature 101.6°F and sore throat, and had already taken quinine and salicylates. The blood-count was as under							
22-7-42	13,200	86.0%	7.7%	6.3%	0.0%	0%	No neo inj taken was well soon again
The last count was done only a fortnight ago as he felt seedy and had premonitory symptoms							
18-9-43	16,000	82.0%	12.33%	4.77%	1.00%	0%	As he was feeling discomfort in chest and abdomen he took one inj of 0.3 gm neosalv after the count, as an abortive measure

CONCLUSIONS

1 One may conclude that the question, whether cases of marked eosinophilia met with in Bombay and other parts of the West Coast of India, and elsewhere form a separate disease entity or not, must be left open for the present. It is quite possible that they are only cases of asthma and allied allergic asthmoid conditions giving an extreme degree of allergic response.

2 The study of my illustrative cases Nos 4 and 6 shows that in spite of an apparent cure after neosalvarsan treatment relapses with recurrence of all the signs and symptoms of asthma-like attacks are to be expected and it would be premature to claim a cure unless the patient remains quite well for over a period of at least fifteen to twenty years, or even longer, as many cases of bronchial asthma in young people are known to be completely quiescent during adult life and only reappear in later life.

3 Neosalvarsan, if given in a course of six injections intravenously, commencing with 0.3 gm, and then continuing with 0.45 gm at weekly intervals, establishes a practical cure which may last for over three years and in some cases even much longer.

4 On the very first day of an attack, the discomfort and other symptoms appear first and the eosinophilia appears afterwards.

5 At the very commencement of an attack, the blood examination may show only a rise in the total leucocyte count without an increase in the relative percentage of eosinophils. In the presence of cough and chest discomfort the rise in the total white count though unaccompanied by eosinophil increase is an indication for giving an abortive dose of 0.3 gm, neosalvarsan, more particularly so, if there is a history of previous similar attacks and of blood-eosinophilia.

DETECTION OF M. TUBERCULOSIS

By

C. B. DHURANDHAR

M. B. S. D. O.

A STUDY OF BLOOD CULTURE IN TUBERCULOSIS AND THE RELIABILITY OF GUINEA PIG INOCULATION TEST IN THE DIAGNOSIS OF HUMAN TUBERCULAR AFFECTIONS

Samples of blood were examined for detection of M. Tuberculosis culturally according to Lowenstein's technique from suspected cases of tubercular diathesis such as phlyctenular conjunctivitis, vitreous hæmorrhages detachment of retina, etc. In the earlier part of the work some difficulties were met with in obtaining growths on Lowenstein's medium but by varying the quantities of various constituents a particular composition of the medium was hit upon which favoured the growth of M. Tuberculosis. The reliability of the technique of laking the blood and digestion was varied by addition of a known number of live tubercle bacilli to normal samples of blood and recovering them in the cultures. As small a number as 50 was sufficient to produce a good growth thus showing that Lowenstein's medium was probably the best medium for the growth of M. Tuberculosis. About 160 samples of blood from cases of trachoma, phlyctenular conjunctivitis, etc. were examined in the following way. 10 c.c. of blood was collected aseptically in 3 c.c. of 10 p.c. sterile sodium citrate solution. This could be preserved in a refrigerator for some days. The sample of blood was thoroughly laked with 40 c.c. of sterile distilled water, centrifugalized at high speed for 20 minutes and the supernatant fluid was thrown off. The deposit was laked twice again with 50 c.c. of water in the same way and was subsequently digested with 3 c.c. of 15 p.c. H_2SO_4 . The acid was removed by washing three times with 50 c.c. of water and centrifugalising for 20 minutes. From the deposit thus obtained a smear was prepared and stained with Ziehl Neelsen method for detection of tubercle bacilli and the rest of the material was inoculated on medium slopes. The tubes were closed either with paraffin or wax and were incubated at $37^\circ C$. From time to time the

tubes were opened and scraped. From a part of scrapings, smears were prepared and the rest was inoculated again on fresh medium slopes (for subculture). None of the smears showed presence of tubercle bacilli. Out of 70 samples of blood from definite cases of pulmonary tuberculosis from the Maratha Hospital, only one showed a positive growth on cultural examination. It was from a case of pulmonary tuberculosis with cavities in the lungs, having sputum with large number of tubercle bacilli and evening rise of temperature. By the time growth was obtained the patient was dead and no further investigation could be done. Thus out of 300 samples of blood, taken from various disease processes, only one showed a positive growth. The experience thus gained was subsequently utilized for detection of tubercle bacilli culturally from other types of material such as pleural fluid, joint fluid, etc. Simultaneously guinea pig inoculations were also performed with the idea of preserving the strain since animal inoculation was supposed to be then 'the court of last appeal'. Out of 12 guinea pigs inoculated with digested material from positive sputa, with large number of tubercle bacilli, 3 animals failed to show naked-eye evidence of tuberculosis on post-mortem examination and subsequent histological and smear examination from suspected material. Surprising as the result was, another experiment was performed with 14 different strains obtained from sputa, blood, pleural fluid, etc. First subculture was used. The animals were more or less of the same weight (300 to 400 gm) and of the same species. These animals were observed from day to day, their weight and temperature were noted and were sacrificed at the end of 3 months except those which died before that period. All of them were subjected to post-mortem examination and histological sections and smears were examined thoroughly for evidence of tuberculosis. Out of 14 animals only 4 died before 5 weeks, the rest had to be killed. Except 2 the rest of the animals showed gradual rise of weight. None of the animals showed rise of temperature above 101° (normal 97° to 101°). On post-mortem examination the animals showed great disparity in lesions. Three showed just few enlarged lymphatic glands, 3 tuberculosis in other organs (only cellular exudate), 5 caseation and 3 extensive caseous lesions. Since the strains used were pathogenic and human in origin, the doses of bacilli were massive. The guinea pigs were more or less of the same weight.

and species, this disparity of lesions could only be explained on the hypothesis that there was definite variation in the virulence of different strains, an observation which requires further confirmation. This experiment might be interpreted to mean that failure of 3 animals to develop tuberculosis in the previous experiment was probably due to low virulence of the strains used. To further substantiate this statement one more experiment was performed with graduated doses: (a) 7 animals were injected with 100 organisms, (b) 34 with 1,000 organisms, (c) 4 with 5,000, (d) 2 with 10,000 and (e) with 100,000 organisms. From group (a) 2 animals developed tuberculosis, from (b) 24, from (c) 3, from (d) 2 and from (e) 2. Thus it is seen that with 100 organisms 10 out of 34 failed to get infected. Out of 41 animals from (a) and (b) 26 developed tuberculosis and 15 did not. This shows that if inoculum contains 1,000 or less organisms, less than 36 p.c. of the animals were infected, i.e., one animal out of three might fail to develop tuberculosis with that dose of organisms.

Conclusions —(1) Septicaemia in tuberculosis is of a short duration. (2) There is probably a variation in the virulence of different strains of tubercle bacilli of same type. (3) Weight and temperature of the inoculated animals is no index of the animal developing infection. (4) Inoculation of 1,000 organisms or less failed to produce tuberculosis in 30 to 36 p.c. of animals. (5) From the diagnostic point of view guinea pig inoculation test cannot be considered as '*the court of last appeal*'.

DISCUSSION

Dr Arthur DeSa said that the unreliability of guinea pig inoculation test in the diagnosis of tuberculosis would make the diagnosis of renal tuberculosis a difficult matter for the surgeon. However in view of the accepted fact that the M. Tuberculosis is often seen in microscopic examination of the urinary sediment (40 p.c. and more of all cases), an assiduous and prolonged examination of the sediment by the pathologist is rendered imperative.

Dr R. G. Dhayagude summing up said that he wanted Dr Dhurandhar to read the paper before the Staff Society in order that members of the staff should realize the futility of carrying out a guinea pig inoculation test, an investigation often requisitioned as it has been described in the text-books as the most sensitive test to detect the presence of tubercle bacilli in pathologic material. Although Dr Dhurandhar's work is now old and greater part of it has been published, the interest in the problem still continued and Dr B. R. Shah was pursuing one aspect of it, viz., the virulence of M. Tuberculosis. Dr Dhayagude narrated the account of a few more experiments carried out as an extension of the work of Dr Dhurandhar and he said that it appeared to be well established that the guinea pigs from these laboratories at any rate were not sensitive to human type of tubercle bacilli and that a large proportion of the animals injected with 1,000 micro organisms failed to develop the infection. In the light of this work he requested the members of the staff not to ask for guinea pig inoculation test but to requisition a cultural examination in its place.

Correspondence

The Editor, *The Indian Physician*, New Queen's Road, Bombay
Sir,

I would be obliged if you could kindly publish the following remarks which are excited by the editorial in the *Indian Physician* Vol II, No 9, September 1943

Whilst the authors of the articles 'Tropical Eosinophilia' (Heilig & Visveswar) and 'Non-tubercular Pulmonary Infiltrations' (Major Owen) clearly recognise the important factors which mark Tropical Eosinophilia as a new disease entity, the editorial is apt to confuse the issue by making "asthmoid bronchitis" and "Loeffler's syndrome" appear synonymous with Tropical Eosinophilia Naegeli, in his 'Differential Diagnosis,' never mentioned this complex of symptoms as the wording of the editorial, "from the above description of the disease given by Naegeli who practised in Zurich" (page 334) may suggest I have myself corresponded with him on this subject and I quote from one letter dated 31-12-36 as follows At this time, the German edition of Naegeli's 'Differential Diagnosis' had been completed Naegeli died in 1938)

"My chief being indisposed, I am authorized to reply to your questions regarding the interesting findings in the disease observed by you We only know of so-called *fleeting* eosinophilic pulmonary infiltrations described lately by Loeffler They are suddenly developing patchy, frequently multiple, pulmonary infiltrations which often show a considerable eosinophilia, They are presumed to be allergic reactions (pulmonary microbides analogous to the skin microbides) probably due to tubercular infection. On the other hand, we have seen cases where aetiologically tuberculosis could be excluded Cases similar to those described by you with an x-ray appearance resembling miliary tuberculosis, *we have, however, never seen*

(Sd) Dr Rohr,

Physician-in-Chief,

University Clinic for Internal Diseases, Zurich "

I had also sent blood films and x-ray pictures of typical cases to two other Continental authorities (Volhard & Morawitz) who informed me that they had never seen such cases or even heard of them

One can hardly mistake Tropical Eosinophilia for one of those diseases to which the citation from Naegeli refers Asthmoid bronchitis is known to have no leucocytosis and only moderate eosinophilia without pulmonary infiltrations In Loeffler's syndrome, clinical and radiological signs always disappear spontaneously within a very short time

Since writing my publication (December 1941), I have treated 45 more cases of Tropical Eosinophilia, all of them so strictly conforming to my original description that none of my statements requires modification

During my five years' practice in Bombay, I have not been aware that this disease was at all known or even under investigation, although I understood later that "asthma" was occasionally treated with Soamin without, however, discriminating between its different types

Lastly, I cannot agree with the opinion expressed in your editorial that a chronic state of Tropical Eosinophilia may exist with the absence of eosinophils in the blood and leading to cardiac and pulmonary failure. On the contrary I have never come across what on the Continent was known as "right sided heart failure" and what lately has been termed "cor pulmonale" in America, as a consequence of Tropical Eosinophilia, where emphysema, which of course, is responsible for this complication, never plays an important part. The case with the longest duration observed by us suffered for over 22 years and had 42,000 WBCs and 64 per cent eosinophils at the time of admission to Hospital in January 1942. There was no indication of even the slightest cardiac complication and arsenic therapy brought about a complete cure, controlled by several examinations since the course of treatment was finished

Yours faithfully,

(Sd) Dr R J Weingarten, M.D.,

Principal Medical Officer,

Bikaner

Bikaner
28-9-1943

"We gladly print Dr Weingarten's letter and, with Heilig and Visveswar, and Owen, readily concede to him the honour of being the first to report a series of cases of eosinophilia with asthmoid bronchitis and pulmonary infiltrates. Our statement is a pure matter of fact which can be easily verified that "asthmoid states" were treated by many Bombay practitioners with intramuscular or intravenous arsenicals and that some of these practitioners obtained reputation as "asthma specialists," perhaps because they were lucky enough to get a large number of patients suffering from "Tropical Eosinophilia" under their care. The treatment, of course, was empirical and the users had no knowledge about the pathological state nor did they differentiate it from other types of asthma

We have referred Dr Weingarten's letter to Dr S K Vaidya a clinical pathologist of Bombay, who has been insistent for many years past, *on the use of neosalvarsan in cases of eosinophilia and in cases suggestive of lymphatism* for his observations, which are printed elsewhere in this issue

In cases recorded as Eosinophilic Leukaemia pulmonary infiltrates are observed by many others. Bass (1931) in recording a case of a Porto Rican boy of 8, who showed a persistent leucocytosis ranging between 26,000 and 47,000 with eosinophilia varying between 32-76

per cent, writes that "coarse râles were constantly present over both lungs, and the roentgenogram *constantly* showed shadows resembling those of miliary infiltrations" (Am J of Dis Child 41, June 1931, p 1395)

He prints roentgenogram of the chest showing irregular mottling in both lungs. He also gives a summary of a case of Armand-Delhille and de Pierredon, a boy of 13, who had spent his early life in Tahiti, where at the age of 8 he had severe malaria, and who had several attacks of urticaria and asthma. He was brought to the Hospital in Paris for asthma. Fine râles were present over both lungs. Roentgenograms showed fine spots resembling miliary tubercles disseminated throughout both lungs. Sputum and tuberculin tests were negative. Blood examination showed 35,000 leucocytes per cmm of which 76% were eosinophils. (Bull Soc de pediat de Paris 25 424 (Oct-Nov) 1927) (Am J Dis Child 41 1399)

In asthma high eosinophil count is mentioned by many authors (Osler, Emerson, etc). Acton and Dharmendra who have studied one hundred and fifty cases of asthma (Ind Med Gaz Apr, 1933) record many cases of eosinophilia. Their observations on the rôle of eosinophils in the diagnosis of spasmodic asthma, (Ind Med Gaz, Aug 1933, p 436) are also interesting.

Greval (Ind Med Gaz Nov, 1940 p 676) in a note on Lecithinophile Eosinophilia which gives a false positive Wassermann reaction which becomes negative with the fall in eosinophils, records two cases observed in 1938 in the Carmichael Hospital for Tropical Diseases. (1) A Hindu, female of 13, had fever, cough and enlarged tonsils. The WR was positive. The eosinophil count was 80%. It fell down to 12% after 'a course of six arsenic injections' and the WR became negative. (2) An Anglo-Indian man of 29 had asthma of 12 years duration. The blood showed eosinophilia of 45%. His WR was positive. He was given peptone injections for asthma. No arsenic given. His WR became negative and eosinophil count fell to 5 per cent.

Stewart (1929-1933) records a case with 100,000 leucocytes and 72-90 per cent eosinophils, in which there was a history of bronchial asthma. Aubertin and Gurnox (1921) record a case, with 6,900 to 26,000 white blood cells of which 70 per cent were eosinophils, who died from cardiac failure due to 'sclerosis of the pulmonary artery' (Quoted from Forkner, Leukaemia and Allied Disorders, 1938, p 178).

The writer has observed these cases with miliary shadows since 1932, and comparing them with the x-ray appearances of the lungs in cases of whooping cough has differentiated them from cases of miliary tuberculosis and given a good prognosis. He uses arsenicals in the treatment of these cases following the well-known usage of arsenicals in blood dyscrasias, and prefers intramuscular of intravenous injections to Fowler's solution by mouth, because of the desire to give the largest possible dose in the shortest possible time compatible with safety.

Now that the syndrome can be recognised as a separate entity from "classical asthma," and from Loeffler's syndrome, may one sug-

gest an intensive search for the "allergen" which produces such a "prolonged allergic reaction" as opposed to the "fleeting" reaction noted in Loeffler's syndrome? One feels with Heilig and Visveswar that a search for a specific "spirochete, spirillum, blastomycetes, or some other organism" will not be in vain. In this connection, it is worth remembering the work done on the gram-negative bacillus —'the asthma bacillus'—(Eyre, Walker (1919), Thomas et al (1924), Acton and Dharmendra, (1933), which is considered by Knott and Oriel (1930) to produce histamine-like substances

—Editor, I P

[A Note —Regarding the case of S S, a policeman, reported in *The Indian Physician*, Vol II, No 9, p 334, the eosinophils fell to 9%, after the sixth injection of neosalvarsan 0.45 gm and he left the hospital with an increase in weight of 6 lbs and free from all symptoms]

Announcement

The All-India Medical Conference will hold its twentieth annual session at Ahmedabad in the last week of December. There will be a scientific section where original papers will be read, and Symposia on different subjects held. There will also be an exhibition of pharmaceutical preparations, surgical instruments and appliances, and botanical plants collected locally or brought from Abu, Pavagadh or Himalaya mountains. Those desirous of attending or of reading papers should get in touch with the Local Secretary, XX All-India Medical Conference, Surgical Hospital, Ellis Bridge, Ahmedabad.

